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PRESENT-DAY STATUS OF POLIOMYELITIS*

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PERIODIC assessment of knowledge regarding infantile paralysis is highly desirable. I know of no other disease in which the public has such a great interest and, in turn, apprehension out of proportion to its incidence, morbidity and mortality. Many sensational statements regarding new developments are reported in the lay press with very little corresponding information available in medical journals and without scientific confirmation. This makes it difficult for members of the medical profession not working in this particular field to keep informed regarding developments, real or alleged, affecting the disease. The public is much more likely to be aware of exaggerated, false claims than of actual scientific advances. Why should such sensational and unsubstantiated claims pervade the atmosphere in this disease?

The nature of poliomyelitis itself is the greatest factor. The disease is extremely variable: in some cases it produces no recognizable paralysis, and in others it causes total paralysis, with all variants in between. The completeness of recovery depends to a considerable extent on the original degree of involvement; yet in the acute, preparalytic stage, it is impossible to estimate the amount of paralysis and disability that will occur. A considerable percentage of patients seen in this stage will recover completely if no specific treatment is given.

The original sampling of patients becomes a significant factor in determining the results obtained in any group of cases. If a report is based upon cases that are included in the series in the preparalytic stage, the results obtained will be statistically very good, since many of the patients will recover completely whatever the treatment they receive, whereas if the group is composed of patients who are admitted in the paralytic stage and of those who are referred when seriously involved, the apparent results will be much less favorable.

It is easy to produce a report indicating that a new treatment is excellent merely by establishing the criterion that the therapy is effective only if given in the preparalytic stage. Since many mild and nonparalytic cases will thereby be included, the recovery on a percentage basis will be excellent.

The problem of evaluating reports is further complicated by the fact that, owing to a chain of circumstances, many people have entered the field of therapy of infantile paralysis with little appreciation of the basic nature of the process and without previous experience.

In a disease of such characteristics, "new treatments" that are introduced are described as changing the prognosis radically. One of these new treatments that has been widely popularized was said to be based upon a new concept of the disease, in which paralysis was relegated to a minor role. This method was reported to be revolutionary in its results and was extensively publicized; this publicity marked the beginning of sensationalism in infantile paralysis, which still continues. Other treatments have been reported and carried to the public without scientific confirmation.

Furthermore, an organization, nationwide in scope, is concerned with raising funds to combat the disease. This keeps the subject before the public, and despite the desire of this organization to educate the public only in scientific facts, such a result is not always obtained. It should be the desire of the medical profession to keep the public informed of scientific achievements in medicine, but this educational program must involve substantiated scientific facts.

Knowledge regarding infantile paralysis is accumulating, not by revolution but by evolution. Research in this field has increased greatly in recent years, largely under the impetus given by the funds of the National Foundation for Infantile Paralysis. Important information has been added, and yet in its practical import the total contribution has been disappointing. This does not belittle the work that has been done or reflect on its necessary character.

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In the field of epidemiology, for example, the usual method of spread of the disease still remains in doubt, although many factors regarding the natural history of the virus are better understood. The presence of the virus not only in the stools of patients and contacts but also in sewage and flies and the evidence of a carrier state tend toward a better understanding of the means by which the disease is communicated. The evidence is that the virus is quite widespread in times of epidemics and that relative immunity, at least to the neurotropic factors of the disease, plays a large part in the epidemiology. This may well be due to the fact that most people have had the disease in the subclinical form. Yet the usual method of transmission still remains unknown. Lack of this knowledge, incidentally, increases the apprehension of the public.

One feature of the epidemiology should be emphasized: the increased incidence of bulbar poliomyelitis in patients shortly after tonsillectomy. Since this is the form of the disease with the highest mortality, tonsillectomy performed during a poliomyelitis epidemic or when endemic cases are occurring is, under ordinary circumstances, undesirable.

It is impossible in a short time to discuss in any detail the recent contributions of research. Electromyography has been of assistance in interpreting the abnormal neuromuscular physiology in the disease. The neurotropic character of the virus and the diffuseness of the involvement of the nervous system have been confirmed and emphasized. However, we are still without a method of increasing either passive or active immunity to the virus. The real advance will come when infantile paralysis can be prevented, but for the present we are confronted with the necessity of treating the disease as effectively as we can to obtain the maximal functional result.

Before therapy is considered, certain clinical features of poliomyelitis should briefly be reviewed, and the pathologic process, so far as it is essential for this discussion, should be considered.

Clinical and Pathologic Considerations

Infantile paralysis is characterized by an acute illness that, in its first phase, may be nonspecific but soon causes symptoms referable to the central nervous system, with increasing sensitivity, spasm and paralysis. Not infrequently, between the early nonspecific portion of the acute illness and the period when symptoms referable to the central nervous system occur, an afebrile stage of from one to five or even seven days may exist, giving a diphasic character to the acute illness. The acute febrile stage of the disease may be very short, but usually lasts from five to ten days, after which an increase in the degree of paralysis is rare. Death, if it occurs, is ordinarily due either to respiratory involvement or to bulbar paralysis.

Paralysis of recognizable degree may or may not be present, and the distribution is extremely variable. It may affect but few muscles; it may affect all. It tends to be regional in its distribution, although a patchy character is common. The effect on individual muscles varies from slight weakness to complete paralysis.

The particular combination of neuromuscular effects that the disease produces causes it to be deforming and disabling. The paralysis is the factor of chief importance, but in the early stage, the spasm contributes to the deformity and in turn to the disability. If one pictures a disease in which one group of muscles may be paralyzed, and the opposite group controlling the part are in painful spasm and shortened, it can be appreciated that deformity will result. This tendency is increased by the fact that carrying the part out of deformity is painful. To add to the difficulty, if parts are left for a period in a deformed position, a secondary myostatic contraction develops, and the deformed position becomes fixed. Furthermore, deformity, as well as sensitivity and muscle spasm, inhibits muscle function and, in turn, the return of muscle power.

Although the effect of the disease on the central nervous system is quite widespread, the main destructive action is on the anterior-horn cells, producing a flaccid paralysis. It should be emphasized that the action on the anterior-horn cells supplying a particular muscle may vary in all degrees up to their total destruction, and hence from temporary neuronal injury with rapid recovery of function to irrevocable paralysis. It must likewise be considered that weakness of a muscle, short of complete paralysis, is due to the involvement of a particular proportion of its neuromuscular units and that even in muscles severely involved one or more residual neuromuscular units usually remain. These, for purposes of therapy, are designated as "guiding contractile units."

If the involvement is severe, the recovery of the power of the muscles extends over a considerable period, but it usually may be said to be completed in sixteen months, with the greatest degree of recovery in the earlier part of this period. In the individual muscle, the prognosis for recovery cannot be anticipated in the early paralytic stage. The greater the degree of paralysis at the start, the less likely is complete recovery of the particular muscle, especially if the paralysis is equally extensive in the regional area.

The pathologic mechanism that produces the sensitivity and spasm remains unknown. Lovett years ago suggested that the involvement of the posterior ganglions might be the factor. The possibility that it is due to effects on the internuncial neurons or on neurons with an inhibiting or stimulating action on the anterior-horn cells has been proposed. It should be emphasized that the spasm

is not the most damaging effect of the disease, as proposed in the Kenny concept, but that it is a symptom that, with sensitivity, tends to be deforming in the early stages. Pain and muscle spasm inhibit muscle function during the acute stage, but the disability of consequence arises from the paralysis. Spasm becomes important in the end result only when paralysis exists.

Treatment

Progress in the therapy of poliomyelitis has been one of gradual evolution based on physiologic principles as applied to the pathologic process. The flurry accompanying the Kenny method has receded. It has stimulated a re-evaluation of technics, and, in fact, in this way it has been most beneficial. Curare and prostigmine have not been demonstrated to be of particular value. Their use is based upon an idea that the spasm is of greater significance than present knowledge can substantiate.

Treatment depends upon the stages of the disease and the degree of involvement. It is best considered by subdividing the disease into three stages — a modification of Lovett's original classification. The first is the acute stage, which may be described as the period of the acute febrile illness, and which may, in turn, be subdivided into a preparalytic and a paralytic phase. The second is the convalescent stage or stage of recovery — the period during which muscles may recover their power — and may be said to end in sixteen months; this may be subdivided into the sensitive phase and the insensitive phase, the first, or sensitive phase, ending when the sensitivity and muscle spasm are no longer present. The third stage (the chronic or residual stage), which follows the convalescent stage, is the period after actual recovery of the muscles is to be expected, although the functional capacities of the patient may be greatly improved during this phase.

Acute Stage

In the acute stage, the treatment is mainly symptomatic. Bed rest is essential, and the patient's activities should be minimal under these conditions. He should not be allowed to wait upon himself. To carry the idea farther: if, in epidemic periods, a patient has a minor illness of nonspecific character that might possibly be the first stage of the diphasic type of onset, his activities should be curtailed for a sufficient period after the temperature has returned to normal to establish the fact that the disease is not present. There is evidence, for example, that fatigue and overactivity during this period, such as swimming in cold water, increase the morbidity of the disease.

With the onset of symptoms referable to the central nervous system, such as sensitivity and spasm, heat in the form of intermittent hot packs may be applied to the sensitive areas as indicated, although prolonged hot packs, which are debilitating, are contraindicated. When paralysis occurs, careful attention to the position of the parts, which must be supported and kept out of persistent harmful attitudes, should be given. Fixed positions for any considerable period should be avoided. Gentle handling of the patient is imperative, and sedation should be used as indicated. Sedatives should not be employed, however, as a substitute for good care.

During the stage of developing paralysis, the patient should be observed frequently for evidence of respiratory involvement or bulbar paralysis. If there are any signs of either type of involvement, constant nursing attention is essential, and the physician must be prepared to meet the emergency.

Bulbar involvement is indicated by such signs as difficulty in swallowing, changes in the voice and irregularity of respiration. Spinal respiratory paralysis is suggested by diminishing respiratory excursion, asymmetric or other abnormal yet rhythmic motions of the chest, use of the accessory muscles of respiration, shortness of breath and cyanosis.

These two types of involvement must be carefully differentiated, since the method of treatment of one is entirely different from that of the other, and to confuse them may result in a fatal outcome. In the bulbar type, the immediate indications are to keep the head dependent to allow for drainage, suction of the pharynx, parenteral feeding and manual aid to respiration if there are transient periods of difficulty. In the spinal respiratory type, the use of a respirator is indicated and may be lifesaving. Only rarely is a respirator indicated in the bulbar type of paralysis, as when the center actually fails completely or when the bulbar form is combined with the spinal respiratory type. Tracheotomy may occasionally be necessary but only on specific indication.

In patients with a fixed elevated chest, continuous local hot packs may be helpful. Feeding by gavage is contraindicated in the bulbar type of the disease if the patient cannot swallow, since vomiting may occur, with disastrous results. Continuous special care is essential in bulbar poliomyelitis since this type has a high rate of mortality that can thereby be greatly reduced. The problem in this type is emphasized by the knowledge that if a patient with bulbar poliomyelitis survives the acute stage, he usually recovers completely. I am particularly pleased to report that the death rate in infantile paralysis at the Children's Hospital, Boston, during the last three years has been slightly under 2 per cent.

Convalescent Stage

The return of the patient's temperature to normal marks no abrupt transition in treatment, but the therapy directed toward the neuromuscular abnormalities becomes more active. In the first phase of this stage, the patient is usually quite sensitive. All handling must be gentle, and motions of the involved parts should be assisted.

Hot packs are continued as indicated to alleviate the spasm, which of itself is deforming. Packs of the lay-on type are most frequently used. These may be applied several times a day and ordinarily are employed only on particular areas where the spasm is deforming and uncomfortable. It is well to add that hot packs have been used at the Children's Hospital during the sensitive stage of the disease for over twenty-five years.

In this stage, more effort is directed toward maintaining the desired anatomic position. Exercises involving gentle passive motions are performed several times daily to carry the position out of deformity and to develop an increasing range of motion. Correction at this stage should not be forced or painful. Parts are maintained in as good a position as possible and supported as necessary. Support to the feet in particular, whether with a portable foot support or a bedboard, is needed. The bedboard with the mattress pulled away from the foot of the bed (Kenny) allows the foot to be maintained at a right angle when the patient is prone. If it is difficult to control a deformity, bivalved plaster splints or wire splints are often indicated, particularly to support the feet. The splints are frequently used only part of the day and at night. This does not in any way deviate from the principle that parts should not be left in one position for long periods and in no way interferes with other factors of treatment.

An estimate of muscle function recording the degree of involvement should be made after the temperature has been normal for forty-eight hours, or shortly thereafter. This should be followed by an accurate "muscle examination" recording the functional power of the various muscles as soon as it can be accomplished painlessly and without disturbing the patient. This often needs to be done in piecemeal fashion. Such an examination is performed at regular intervals to record the progress of recovery. Active exercises are based on this examination.

Active guided exercises are added early on a graduated scale, discomfort and fatigue being avoided. These active exercises follow the principle that the weak muscles are required to carry out their function without allowing other muscles to substitute for their action. If a muscle cannot perform the action, the action is performed with a therapist assisting in the motion but with the patient making every effort to use the muscle. The position of the exercise varies according to the strength of the muscle and the function that can be elicited in the particular position.

These active exercises are based both on empiric observations and on physiologic principles. It is recalled that anterior-horn cells may be involved to any degree and that their function may be lost for a considerable period without death of the neuron and with consequent recovery of function. Furthermore, if a muscle is left out of a particular pattern of motion for a period, it may recover its potentiality of function without returning to the pattern. During the convalescent stage when recovery is possible, it is quite important to maintain by exercises the action of the paralyzed muscle. If the weak muscle is not protected and stimulated to contract, and instead indiscriminate substitute motions are performed at all times, the weak muscle may drop out of the pattern completely. In this connection, it is well to remember that guiding contractile neuromuscular units exist for most muscles, even those severely affected. If all anterior-horn cells have been destroyed for a particular muscle, active exercises for this muscle are of no consequence. This, however, cannot be foretold during the earlier part, at least, of the convalescent stage.

Underwater therapy is highly valuable in the sensitive stage as well as in the later period of convalescence. The Hubbard tub is used early with the water at as high a temperature as is tolerated comfortably by the patient. This decreases the spasm and sensitivity and aids, with exercises in the water, in developing a range of motion and in correcting deformities. As the sensitivity decreases, exercises in a tub with water at a lower temperature and, in turn, in a pool, are of great assistance, particularly in patients who have considerable involvement.

Insensitive phase. After the insensitive phase of the convalescent stage is reached, actual stretching of the contracted parts is often necessary, and the active exercises are increased as tolerated. The first problem is to get the patient to use the afflicted muscle properly. Later, exercises are added that increase strength and produce hypertrophy. Part-time support for parts with deforming tendencies is often still needed.

Sitting and standing are ordinarily instituted in this stage also. This transition must be carefully supervised, and one must make sure that these activities are performed with as good a balance as possible without deformity being increased, and determine that the various muscles are used in as normal a functional pattern as possible. Crutches are often a desirable aid in walking at the start, depending upon the involvement of the arms. Walking braces are not ordinarily used during the convalescent stage until the maximal recovery of muscles has occurred, provided that the patient, when ready to walk, is able to walk without inducing further deformities. Walking of itself is an essential exercise if properly performed. Walking braces may be used during the latter part of the convalescent stage when it becomes apparent that they are necessary for effective locomotion. In the chronic stage, a brace should be used at least part time if the patient can walk more effectively with it than without it.

Chronic Stage

In the chronic stage, the problem is to make the patient as effective as possible, despite the residual involvement. Particular cases may need regular stretching of certain parts. Muscles of borderline strength may need exercises designed to produce hypertrophy. Occasionally, support of one kind or another is needed for use at night.

Functional and gait training are most helpful in this period, particularly in patients who have had severe involvement or who have not been well supervised in their early course. Whereas, in the convalescent stage, muscle substitution is prevented, in this stage, if it is necessary, it is cultivated and supervised to produce the best function despite the paralysis. The adult may require little supervision in the chronic stage unless he has very extensive involvement, whereas the child with residual involvement should be supervised regularly during the growing period, since deformities may progress, owing to disturbances in growth.

It is also in the chronic stage that operative intervention may be indicated in such forms as tendon transplantation to supply a needed muscle function, fusion of parts by arthrodesis or corrections of deformities and improvement of function by other surgical means. Considerable progress has been made in the operative rehabilitation of patients in recent years.

* * *

The treatment of infantile paralysis may be very simple in patients with mild involvement, and the outline of therapy presented above is interrupted as indicated. In a small percentage of cases it is a long, arduous task requiring highly skilled, patient, physical therapists and careful medical supervision by those experienced in the disease.

Ideally, it is believed that the patient with acute poliomyelitis should be supervised from the start by a team composed of a pediatrician or internist and an orthopedic surgeon, or at least someone experienced in the care of the musculoskeletal system in this disease. Attention must be given to the care of the musculoskeletal system from the start, thus preventing deformities and complications and simplifying the later treatment.

All patients, from the onset of the disease, are best cared for in a hospital. This would not necessarily be true if it were not for the possibility of a bulbar or respiratory paralysis. However, transportation of patients for long distances during the acute febrile stage should ordinarily be avoided.

Since an epidemic may occur at any time, one must be prepared to care for patients in the acute stage in local hospitals. After the febrile stage, if there is much involvement, treatment may be necessary in a special unit with an adequate staff of experienced physiotherapists, under proper supervision. It is well to recall that death, if it occurs, is most likely to happen during the acute stage; and the hospital caring for the acute disease must be prepared to give the best of supervision in this stage. In a large percentage of children the treatment after the sensitive period of the convalescent stage can be carried out at home if the mother is carefully instructed regarding the exercises and routine of care, and provided the child is supervised at regular intervals by the physician and physical therapist. The expense of care can thus be greatly decreased.

Knowledge of infantile paralysis is increasing, and therapy in the disease is improving, but not by any revolutionary discoveries.

THE TREATMENT OF POLYCYTHEMIA VERA BY SPRAY IRRADIATION*

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IN 1932 the treatment of polycythemia vera by spray irradiation was instituted at the Massachusetts General Hospital by the Department of Radiology at the suggestion of Dr. Francis T. Hunter. The results of treatment at the end of a ten-year period were presented by Robbins.[1] The purpose of this study is to report upon the present status of the original group of patients and also upon the results of treatment in 8 additional patients. This method of treating polycythemia vera has proved the most successful of any of the procedures that have been tried at this hospital, and it has seemed worth while, for the benefit of the clinician, to re-emphasize its value.

Irradiation of the bone marrow in cases of polycythemia vera was first suggested in 1907 by Stengel.[2] Lüdin,[3] in 1916, was the first to treat the disease successfully by irradiating the long bones of the skeleton. In 1932 Sgalitzer[4] reported good results from irradiation of the entire body. Similar reports followed from Hunter[5] and Sanderson[6] in 1936 and from Pierson and Smith[7] in 1940.

The investigations of Lawrence and his associates[8, 9] and others[10, 11] on the use of irradiated phosphorus suggest that in the future this may be the treatment of choice in polycythemia. The advantages of its administration are threefold: it causes less discomfort to the patient, its administration is easy, and it takes less time than irradiation by x-ray. On the other hand, a universal standard for measurement of radioactivity is lacking, and its long-range effects are still unknown. Radioactive isotopes, even though the "half-life" may seem safe, introduce a form of radioactivity whose long-term effects cannot yet be predicted. The same criticism may be applied to spray irradiation and may account for the reluctance of some physicians to make use of it. The experience at this hospital has been limited purposely to the use of the latter form of treatment because of its apparent success, and to keep this series of cases intact. The time may come, however, when radioactive isotopes will prove to be of greater value.

It is the policy of the hospital not to use any form of prolonged irradiation, whether for diagnosis, treatment or study, in persons who are not sick or who have a self-limited or benign disease. Polycythemia, however, whether neoplastic or not, invariably ends fatally and must be considered and treated as a malignant disease.

METHOD OF TREATMENT

Spray irradiation is given with the intention of covering a field extending from the neck to the knees of the average person. This requires a long target-skin distance, which varies from 215 to 250 cm., and can usually be accomplished with a 20-by-20 cone on the machine. The area is centered at the level of the crest of the ilium, and anterior and posterior fields are treated on alternate days.

The following factors have been found satisfactory: kilovoltage of 200, 0.5 mm. of copper and 1.0 mm. of aluminum filtration, which gives a half-value layer of 0.92 mm. of copper. The daily dose varies from 20 to 30 r, measured in air, and the total dose is approximately 300 to 500 r in any one series of treatments, divided between an anterior and a posterior field. The small daily dose usually prevents severe roentgen-ray sickness, and the repeated small assaults on the bone marrow may have a more prolonged effect than larger daily doses. Some of the first patients treated received larger daily doses and larger total doses, but the method outlined above has seemed to be safe and satisfactory. It produces fairly prolonged remissions without causing incapacitating radiation sickness, and with these doses there has been, with one possible exception, no definite injury to any of the patients.

The amount of treatment is determined by the total white-cell count. Such a count is taken at the beginning of treatment, at the end of a week, and at shorter intervals as the cells decrease; toward the end of treatment daily counts are taken. When the count falls below 5000 to 6000, treatment is stopped. No particular attention is paid during treatment to the red-cell count or to the hemoglobin level, since these determinations usually do not change significantly until a month or two after the treatment has been completed.

Tables 1 and 2 give the over-all results in 28 cases of polycythemia vera. To summarize the available data in a not too cumbersome form, certain laboratory findings, such as hematocrit determinations and oxygen-capacity studies, have been omitted. In the opinion of some investigators hematocrit determinations are considered indispensable in the treatment of patients with polycythemia vera. Experience in this hospital has shown, however, that the total clinical picture, together with white-cell and red-cell counts and perhaps photoelectric hemo-

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globin determinations, are sufficient and require considerably less time.

Twelve patients died, as compared to 16 who are alive. These results do not seem impressive until the causes of death are analyzed; many of the deaths were due to conditions other than polycythemia. Furthermore, this disease typically occurs in elderly persons, in whom life expectancy is short. In none of the group did leukemia, a leukemoid state or so-called "myeloid metaplasia" develop.

Table 3 presents details regarding the fatal cases. Two patients died of pulmonary disease apparently not related to polycythemia, 1 died of carcinoma of the breast two years after its discovery and eight years after irradiation for polycythemia had been started, and 1 died of uremia due to prostatic obstruction. It is not believed that these deaths were due either to the polycythemia or to its treatment.

Six deaths were caused by arterial thromboses (3 coronary, 2 cerebral and 1 cerebral, aortic and subclavian) and can be attributed to the primary disease. One patient died of pulmonary embolism two weeks after the beginning of irradiation. The cause of death in another case is unknown, but it is attributed to polycythemia.

It is difficult to assess the effect of polycythemia vera in producing vascular disease. Obviously, relatively few patients in this age group who develop vascular disease such as cerebral and coronary thrombosis have polycythemia. On the other hand, an untreated patient with polycythemia usually dies of vascular disease. Four of the patients who died from such causes may actually have died because of insufficient treatment.

The status of the 16 living patients is presented in Table 4. Thirteen have no symptoms attributable to polycythemia. One patient has a dangerous

TABLE 1. *Status of 28 Patients with Polycythemia Vera as of December, 1946.*

STATUS OF PATIENT	NO. OF CASES	INTERVAL SINCE FIRST TREATMENT		AVERAGE AGE AT TIME OF DEATH
		RANGE	AVERAGE	
		yr.	yr.	yr.
Living	16	1.5–9.0	5.4	—
Dead	12	1.5–11.0	5.6*	65.2

*Omitting 2 patients who died during treatment.

TABLE 2. *Pertinent Data in Entire Series.*

HOSPITAL NO.	CASE NO.	SEX	AGE AT ADMISSION	TOTAL IRRADIATION	NUMBER OF COURSES	RED-CELL COUNT			INTERVAL SINCE FIRST TREATMENT	REMARKS*
						MAXIMUM	MINIMUM	FINAL		
			yr.	r		$\times 10^6$	$\times 10^6$	$\times 10^6$	yr.	
65650	1	M	52	3680	6	10.6	4.25	4.25	11.0	Death from lung sepsis
10879	2	F	49	1500	3	8.1	4.4	5.8	7.5	Sudden death (? coronary disease)
129760	3	F	38	600	1	7.3	3.7	6.05	7.5	Inoperable cancer of breast 2 yr. before death
323381	4	M	54	600	1	8.85	5.9	7.29	4.0	Patient failed to return for follow-up; death from cerebral thrombosis.
30403	5	M	62	1000	2	6.6	4.9	4.9	6.5	Death from uremia due to prostatic obstruction
8589	6	M	65	1000	2	9.9	7.2	7.2	0.0	Death 2 months after beginning of treatment (2nd series)
40086	7	F	50	1260	3	8.1	4.0	4.29	9.5	Very questionable exposure to benzene; patient well.
115023	8	M	62	1600	3	7.9	4.8	4.8	5.0	Death from cerebrovascular disease
142886	9	M	55	1675	2.5	6.9	4.6	4.69	8.0	Threatened gangrene, subsiding
175527	10	F	70	700	2	8.9	4.2	4.76	4.5	Death from coronary thrombosis
163704	11	F	65	650	1	7.7	4.33	5.8	5.0	Death from cerebral and aortic thromboses
198686	12	F	61	900	2	7.1	2.02	4.16	7.0	Patient well
215738	13	M	47	3200	6	9.2	6.8	9.0	7.0	Unsatisfactory result; patient alive.
226399	14	M	64	500	1	7.7	3.7	5.9	7.0	Treatment refused 8/30/43; patient seems well.
253145	15	M	53	250	0.5	8.3	5.21	5.92	3.5	Incomplete treatment; death from (?)coronary thrombosis.
270452	16	F	37	1400	3	7.5	3.3	4.26	6.0	Dizziness regardless of red-cell count; patient alive.
287060	17	F	57	500	1	7.4	4.19	4.96	5.5	Patient well
206930	18	M	40	1230	3	10.5	2.3	4.42	5.5	Blood pressure of 220/130: patient who refuses hospitalization, alive.
324094	19	F	76	180	0	10.5	—	—	—	Death in bed 2 wk. after beginning of treatment (? embolus).
126422	20	M	76	320	1	9.0	4.65	4.65	1.5	Death in nursing home, cause unknown; probably polycythemia.
353441	21	M	15	700	2.5	9.8	5.3	6.34	3.5	Patient very young; no congenital heart abnormality; no benzene; patient alive.
358968	22	F	34	720	2	8.8	4.3	4.3	4.5	Amenorrhea, probably due to irradiation; patient alive.
396617	23	F	70	400	1	7.55	3.93	3.93	4.0	Venesection (2000 cc.) year before treatment; patient well.
2329	24	F	48	950	3	9.0	2.2	2.2	5.0	Increasing anemia; "marrow fibrosis"; (?) benzene; patient alive.
348906	25	F	65	375	1	7.25	4.5	5.09	4.5	Patient well
364463	26	M	60	1650	4	9.97	5.6	4.7	4.5	Patient well
495384	27	M	53	400	1	8.92	5.06	5.06	1.5	Patient well — (?) exposure to benzene
43567	28	M	34	600	2	6.69	4.22	4.22	3.5	Patient well

*Statements regarding survival apply to patients' status as of December, 1946.

hypertension for which sympathectomy was advised but was refused; the blood picture is normal. Since the report published in 1944 another patient has developed an unexplained, refractory anemia, which must, for the present, be attributed to irradiation.

Table 5 represents an attempt to estimate the amount of irradiation that will provide a maximum remission. The possibility of a cumulative effect of previous irradiation has not been excluded, and the data are hardly sufficient to provide a statistical basis from which to draw conclusions. In general, it appears that the larger the total x-ray dosage, the longer the remission. The size of the dose, however, is limited by an increasing tendency to leukopenia.

TABLE 3. *Data in Fatal Cases.*

Case No.	Final Red-Cell Count	Final White-Cell Count	Final Hemoglobin	Age at Death	Remarks
	x10³		*gm./100 cc.*	*yr.*	
1	4.25	—	11.3	63	Cause of death undetermined; hemoptysis; bronchiectasis demonstrated by x-ray study; last blood smear that of sepsis; patient died 11 years after first treatment.
2	5.8	7,500	19.5	58	Sudden "coronary" death 7½ years after first treatment.*
3	6.0	11,300	16.4	46	Six years after first irradiation patient found to have inoperable cancer o breast; death 2 years later.*
4	7.29	—	—	58	Patient died 4 years after treatment; cause of death, cerebral thrombosis.*
5	4.9	6,900	14.3	68	Patient died 6½ years after first treatment; cause of death, uremia due to prostatic obstruction.*
6	7.2	1,300	—	66	Patient died 6 weeks after completion of second course of therapy; headache, fever, hemoptysis; lung cavities demonstrated by x-ray study.*
8	4.8	—	—	71	Death of cerebrovascular disease in state hospital 5 years after first treatment.* No autopsy.
10	4.76	8,000	16.4	73	Patient died outside hospital 4½ years after first treatment; cause of death, coronary thrombosis.
11	5.8	—	15.5	69	Death 5 years after first treatment; autopsy revealed thromboses of cerebral aortic, subclavian and carotid arteries, as well as gangrene of right arm.
15	5.9	—	18.4	56	Patient died 3½ years after first treatment; ? myocardial infarction; ? insufficient treatment.*
19	10.5	22,000	23%†	76	Patient found dead in bed 2 weeks after beginning of treatment; cause of death, probably pulmonary embolus; no autopsy performed.
20	4.65	8,600	13.0	78	Patient died in nursing home 1½ years after first treatment; cause of death unknown — probably polycythemia.

*Patient died outside hospital; no autopsy performed.
†Sahli.

In this case benzene (benzol) may have been a causative factor of the disease, but in spite of this fact and the possibility that irradiation was responsible for the present anemia, irradiation would have been considered the treatment of choice. One patient, although still alive after seven years, has numerous symptoms and an increased red-cell count, and this case is considered a therapeutic failure.

TABLE 4. *Status of 16 Living Patients (as of December, 1946).*

Case No.	Final Red-Cell Count	Final White-Cell Count	Final Hemoglobin	Interval Since First Treatment	Remarks
	x10³		*gm./100 cc.*	*yr.*	
7	4.29	7,200	13.6	9.5	Headache and hypertension (blood pressure of 180/130) on admission; patient now well; blood pressure, 130/90.
9	4.69	10,500	13.6	8.0	Threatened recurrence of gangrene of toe (present on admission); subsiding; patient otherwise well.
12	4.16	—	14.2	7.0	Dyspnea, weakness and duodenal ulcer on admission; subtotal gastrectomy performed on 10/30/42; polycythemia recurred and treated; patient now well.
13	9.00	7,800	21.2	7.0	Patient unco-operative, unsatisfactory clinical result.
14	5.93	—	18.1	7.0	Gangrene of right foot; amputation; patient now apparently well.
16	4.26	7,200	14.4	6.0	Dizziness regardless of red-cell count; patient otherwise well.
17	4.96	7,300	14.9	5.5	Dizziness and transient paralysis on admission. Patient now well.
18	4.42	—	11.0	5.5	Headache and epistaxis on admission; blood pressure of 170/110; now headache and blood pressure of 220/130; house admission for (?) sympathectomy refused.
21	6.34	—	14.9	3.5	Youngest patient; (?) ruptured spleen on admission; "fainting spells."
22	4.30	—	13.2	4.5	Amenorrhea (probably due to radiation); patient otherwise well.
23	3.93	8,400	12.4	4.0	Throbbing headache on admission. Now well.
24	2.20	2,200	7.0	5.0	Weakness and fatigue on admission. Well until August 1946 when increasing anemia occurred. Marrow biopsy "myelofibrosis."? Benzene; ? anemia due to treatment.
25	5.09	—	14.3	4.5	Weight loss on admission. Now well.
26	4.70	15,600	12.2	4.5	Memory difficulty on admission. Benzene exposure. Now well.
27	5.06	8,400	17.5	1.5	Lack of left-hand co-ordination on admission. Now well.
28	4.22	5,900	17.8	3.5	Headaches and nosebleeds on admission. Now well.

The table suggests that a total dosage of between 400 and 500 r will produce good results.

The total white-cell count has proved the best criterion for determining the amount of irradiation

to be given. When the total count falls below 5000 treatment is discontinued. A count of 1800 or less has resulted from some of the larger doses, but there have been no symptoms and no fatalities from this cause. Especially during the early years of this type of treatment, some patients who received a relatively large dose experienced unusually long remissions of symptoms.

Discussion

The treatment of polycythemia vera by bloodletting is physiologically unsound for several reasons. Blood loss is known to be one of the greatest stimuli to bone-marrow activity and blood-cell production. Such a procedure relieves only one of the complicating factors — namely, increased blood volume; it does not affect platelet production, except by increasing it, and may have no effect in preventing vascular thrombosis. Most patients treated by this method are never quite well even when frequently bled; they need so much medical attention that they consider themselves, and are considered to be, chronic invalids. Phlebotomy eventually results in a condition of plethoric anemia, or hypochromic polycythemia, which is incompatible with good health. Finally, many of these patients develop a condition, variously described as "leukemia," "leukemoid state" or "myeloid metaplasia," which ends fatally.

An example of this is the case of a private patient, not included in this series, who was referred for treatment, after repeated phlebotomies, because of gangrene of the fingers. The blood picture was that of extensive extramedullary hematopoiesis ("myeloid metaplasia") with a severe hypochromic polycythemia, a white-cell picture suggesting myelogenous leukemia and vastly increased platelets. The fingers healed after one course of spray irradiation; the blood picture returned to normal after two courses; but a fatal anemia developed after a third course, two years later, made necessary by a recurrence of impending gangrene in the fingers and by a greatly increased number of platelets. The patient refused to re-enter the hospital for transfusions and further study, and died at home.

Phlebotomy may be indicated, however, for the immediate relief of acute symptoms or when disaster threatens.

Difficulties in the use of phenylhydrazine are well known and require little comment. One of the greatest is in regulating the dosage, since not only do different persons react very differently to the drug but also a single patient may react unpredictably to a constant dosage. Its advantage (or disadvantage?) over phlebotomy lies in the fact that materials necessary for the synthesis of hemoglobin are conserved, and "hypochromic polycythemia" does not develop so readily. The use of this drug has largely been given up.

Theoretically, the use of spray irradiation seems to be a sound approach to the problem since it aims to inhibit an overproductive bone marrow. The results in this series of patients tend to confirm this theory, many of the patients having normal blood pictures for long periods after treatment. A great advantage of this type of irradiation is that patients so treated are perfectly well, often for years, requiring little medical attention, except for an occasional checkup of the blood picture. Another advantage is the fact that it does not produce a plethoric hypochromia and does not end in "leukemia" or "myeloid metaplasia." Vascular thromboses appear to be checked, and life may be prolonged, perhaps for a considerable time. The data in this study, however, are obviously insufficient to justify any positive statement. (The deaths of 6 patients from vascular disease are discussed above.)

The disadvantages of spray irradiation, pointed out above, are: the suffering caused by roentgen sickness; the time and effort consumed in completing a course of treatment; the possibility of producing a refractory anemia (one of the 28 patients treated has such an anemia, possibly or probably due to treatment); and the possibility of deleterious, long-range effects. Except for the patient with anemia and the possibility (rather farfetched) that carcinoma of the breast developed in another case as a result of roentgen irradiation, none of the group developed any such condition.

Table 5. *Effects of One Course of Spray Irradiation.*

X-Ray Dosage r	Patients without Remission	Patients with Remission							
		0.5 yr.	1 yr.	1.5 yr.	2 yr.	3 yr.	4 yr.	5 yr.	6 yr.	8 yr.
1200	—	—	—	—	1	—	—	—	—	—
900	1	—	—	—	—	—	1	—	1	—
700	—	—	—	—	—	1	—	—	—	—
600	—	—	1	—	—	1	—	2	—	1
500	—	2	2	—	3	—	3	2	—	—
400	—	1	1	4	4	4	1	—	—	—
300	—	2	3	—	1	1	—	—	—	—
200	—	1	1	—	—	—	—	—	—	—

A statistical presentation of the results does not give a clear picture of the actual value of this form of treatment. The following of individual patients over a number of years, however, is very impressive; the results in a small group of private patients, not included in this report, are even more impressive. The following case is an example.

A 61-year-old woman with polycythemia was first seen in 1936. At that time she had numerous complaints, especially a severe type of peripheral neuritic pain. The red-cell count was in the vicinity of 11,000,000. In the past 11 years she has received four courses of spray irradiation, totaling 2100 r, and has remained entirely well. She is now 72 years old.*

Although this is but a single case, no comparable result has been found in the reports of those advocating phlebotomy.

Further evidence of the value of spray irradiation therapy derives from the fact that it is resorted to when bloodletting has nearly resulted in death. Three such private patients have been seen at this hospital, 1 of whom died of anemia two years after spray treatment had been begun but who enjoyed better health during that period than he had for many years previously. A second patient, who had a very abnormal "leukemoid" blood picture with hypochromic polycythemia following many years of repeated phlebotomies, is at present well (two years after treatment), with a normal blood picture. The third patient is just completing his first course of treatment. It is not satisfactory to irradiate such patients with abnormal blood pictures due to long-continued bloodletting; they should rather be treated from the beginning by spray irradiation.

Another private patient not included in the group was discovered to have polycythemia vera as a cause for extensive venous, and probably, peripheral-artery thromboses. Bloodletting became impossible because of venous thromboses at the site of the venepuncture. The man was told that nothing more could be done for him. At that time, two years ago, a single course of spray irradiation was given. There has been no subsequent recurrence of thrombosis, and there has been a considerable improvement in the venous circulation.

It should be emphasized that spray irradiation may be a particularly dangerous form of therapy if employed injudiciously. Its use in patients whose increase in red-cell count and in hemoglobin is due to anoxia might prove fatal. Polycythemia vera, as the name implies, is a disease associated with a considerable increase in all the cells of the blood. This is not true of secondary polycythemia or "erythrocytosis." Spray irradiation should never be used in cases of extramedullary hematopoiesis ("myeloid metaplasia") in which the marrow itself has been replaced by tumor or other tissue, for the results may well be fatal. Finally, the not too uncommon, benign condition of familial hypochromic polycythemia, largely confined to members of the Italian race, should never be treated by irradiation. In fact, these patients need no treatment of any kind.

For the reasons stated above, radioactive isotopes have not been used in the treatment of polycythemia in this hospital, and for the moment judgment on this type of therapy is reserved.

*Since this paper was submitted for publication, this patient has died of a condition clinically and pathologically indistinguishable from acute myelogenous leukemia.

Summary

Twenty-eight cases of polycythemia vera treated by spray irradiation are reported.

Twelve patients are dead; 4 died of causes other than the polycythemia or its treatment.

Of the 16 living patients, 13 are free of symptoms attributable to polycythemia, 1 has hypertension, 1 is anemic, and 1 is still polycythemic and is considered a therapeutic failure.

One patient has a refractory anemia, possibly or probably attributable to roentgen-ray treatment.

No patient has developed leukemia, a "leukemoid state" or "myeloid metaplasia."

Phlebotomy is contraindicated in polycythemia vera except in the treatment of acute symptoms or impending disaster.

Spray irradiation is the treatment of choice.

The use of radioactive isotopes is discussed only briefly.

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OVARIAN CONSERVATION DURING SURGERY

With Reference to Bilateral Dermoids and Endometriosis

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CONSERVATION of portions of the ovary during surgery is not a difficult procedure, and yet it is not practiced commonly by general surgeons. Gynecologists are well acquainted with the fact that a very small amount of ovarian tissue will protect the patient's future well-being. Surgeons of lesser training and experience in this specialty are more likely to remove ovaries, probably because of a lack of knowledge of pathology. With increased information on this score, surgeons will remove fewer ovaries in toto and will make every effort to save as much ovarian tissue as possible.

This paper, therefore, is written to call attention to the benefits to be derived from resection, to supplement an article presented in 1939[1] and to make a plea for greater conservatism on the part of the surgeons dealing with ovarian surgery.

In the paper referred to, the case of a thirty-three-year old patient was discussed.† The ovaries in this case were nearly the size of large oranges because of bilateral dermoid cysts. At operation, the right ovary was completely removed. The left was resected; a piece 1.5 cm. in diameter and as thin as a dime remained.

The pathological report, by Dr. M. F. Vidoli, was as follows:

> The first specimen consisted of an ovarian cyst measuring 2.8 by 2 by 1.5 cm., and separately received with the same specimen, a small, irregular, tooth-shaped section, measuring 8 by 6 by 4 mm. Multiple sections showed the entire ovary to be replaced by a cystic cavity filled with greasy, yellowish material and two small cysts, each measuring 6 mm. in diameter, filled with clear fluid.
>
> The second specimen included an oval, smooth, yellowish-gray mass of doughy consistence, measuring 8 by 6 by 5 cm. Multiple sections demonstrated a large cystic cavity filled with yellow, greasy material and a moderate amount of hair. Along one side, the wall became thicker, showing remnants of ovarian tissue and several smaller cysts filled with whitish gelatinous material.
>
> The microscopical diagnosis was bilateral dermoid cysts of the ovaries.

Since the operation, which was performed on July 26, 1938, the periods have occurred regularly without undue event. Frequent pelvic examinations have disclosed no change in the residual ovarian tissue. This finding is entirely consistent with the opinion expressed by various pathologists that normal-appearing tissue is normal ovarian tissue, microscopically, in every respect. What is the rationale for removing both ovaries in such cases? Why cause a complete menopause in a young woman? Why deprive a young woman of the possibilities of having children?

With these thoughts in mind, when a second patient with bilateral ovarian dermoid cysts presented herself, she was also treated conservatively. The subsequent history in this case‡ provides such a direct answer to the questions asked above that the pertinent facts are related as follows:

> During December, 1936, F. W., a 28-year-old woman, reported for a premarital examination. She suspected no physical abnormalities since she had been in good health and since the menses occurred every 28 days and were of 3 days' duration. When informed of the presence of bilateral ovarian dermoid cysts and the possible consequences of the operation, she postponed her marriage and was operated upon on January 23, 1939.
>
> The findings were strikingly similar to those in the case presented above. The right ovary was nearly the size of a large orange and was completely removed along with the tube that was attached to it. The left ovary was likewise enlarged. A small piece of normal-appearing ovary was located near the ovarian vessels. It was "shaved off" and examined for bleeding. Since a slight ooze only occurred, this piece was not further disturbed. As in the previous case, it was hardly as large as a dime.
>
> The pathological report by Dr. H. E. MacMahon was as follows:
>
> One specimen, consisting of an encapsulated structure, roughly round, measuring 7 by 5.5 by 5.5 cm., is pale, yellowish pink. Along one side is a scarred projecting nodule, suggesting ovarian tissue. Section through this reveals a small follicular cyst (regressing corpus luteum). Section through the large mass shows a cavity filled with cornified epithelium. This can be peeled with some difficulty from the wall, leaving a smooth glistening surface. At one point, there is a small bony, hard spicule. In another, there is a small cyst filled with gelatinous mucus-like material. The gross diagnosis is epidermoid cyst.
>
> The second specimen includes a similar cyst, which is roughly round, rather soft and buttery. There is one small, bare area. The wall measures 0.1 to 0.2 cm. in thickness. The cyst is filled with buttery, white material that can be easily removed, leaving a clean surface with the exception of one point where there is a projecting nodule from which a large tuft of black hair protrudes.
>
> The microscopical diagnosis of the first specimen is epidermoid cyst of the ovary, with a small follicular cyst, and that of the second, dermoid cyst, showing skin and skin appendages, cartilage, smooth muscle and abundance of myelinated and nonmyelinated nerve fibers: ganglion cells of the sympathetic system. There is no evidence of malignant change.

Two weeks after the operation, a regular period occurred. After this reassuring episode, the patient completed her plans for marriage. Nine months after the operation, she skipped two periods and then flowed profusely. There was some question whether she had had a miscarriage. Subsequently she was delivered of healthy well formed babies on October 24, 1940, December 22, 1944, and October 13, 1946.

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†Cambridge Hospital Case S-38-518 (July 6, 1938).

‡Cambridge Hospital Case S-39-57 (January 23, 1939).

These cases demonstrate that adherence to the advice in the older textbooks "to remove both ovaries in cases of bilateral dermoid cysts" not only is unwise but also may be calamitous.

As a matter of fact, papers have appeared only recently, urging conservative ovarian surgery in such cases. An extensive search of the literature disclosed few such articles. Usually, reference to the use of conservatism is hardly more than perfunctory. So little is said that unless one is particularly interested, it is taken for granted that radical surgery is the technic to be employed in all cases of bilateral ovarian dermoid cysts.

Geist[2] presents photographs of a dermoid cyst resected from an ovary. Study of this illustration is interesting because it discloses a very wide resection. It seems that in his case much more normal tissue was found and retained than in either of the 2 cases described above. This photograph again emphasizes the fact that one must have the will to preserve normal tissue.

Martzloff[3] describes a case of a thirty-nine-year-old woman from whom, at operation, he removed the left tube and ovary, resecting the right ovary. In describing this case, he states that the right ovary was about twice the normal size. It contained a yellowish cyst, through the wall of which some hair could be seen. This cyst was resected, what would correspond to about a third of a normal ovary being left in situ. The pathological report stated that section revealed a cystic structure filled with sebaceous material in which there was some hair. The author finally commented that when last heard of the patient "had been menstruating normally at twenty-six-day intervals."

This case affords a good illustration of the possibility of conserving the ovarian function when some normal tissue is present, the danger and inconvenience of a premature operative menopause being thereby avoided.

It is interesting to note how casually Martzloff comments on avoidance of a premature operative menopause. I believe that his statement bears greater emphasis because this patient was already near the menopause (age thirty-nine) and yet the author thought in terms of preventing such an occurrence earlier than it would have taken place naturally. This is the type of reasoning that more surgeons should follow. I can say, regretfully, that I have heard many surgeons remark at operation that the patient was near the menopause, anyway, and that the ovaries would be removed "to prevent trouble later on." Such loose thinking, in my opinion, is as illogical as extirpating an eyeball from the surface of which a cinder has been removed "to prevent trouble later on."

Martzloff concludes: "Out of a total of some 200 patients who have had dermoid cysts in one or both ovaries (confirmed by examination of micro-sections) we have had only one other case (two altogether), of carcinoma developing in an ovarian dermoid cyst." (His reference is to cases at the Johns Hopkins Hospital.) This remark can well be appreciated for the important reason that it disproves so effectively what is written in textbooks as dogma: that most ovarian dermoid cysts become malignant, which they obviously do not.

Furthermore, Marshall,[4] in a brief report, presented evidence on 415 cases of dermoid cyst, examined at the Mayo Clinic. Among other facts, he disclosed that in this series 1.9 per cent were malignant. Bell[5] believes that few surgeons give any consideration to the surgical treatment of innocent neoplasms other than the complete removal of the organ and states that, as a rule, some healthy portion of ovary can be preserved with its normal connections, for nearly every neoplasm tends to grow away from the hilus and the preservation of this, with adjacent ovarian tissue, leaves well nourished and functional tissue. Mathews[6] also emphasizes the wisdom of conserving ovarian tissue and points out that the line of cleavage between the cyst and ovarian tissue can easily be followed. Miller,[7] in a general discussion of 90 cases of ovarian dermoid cyst, concludes that conservation of ovarian tissue by enucleation of the dermoid cyst is an easy and valuable procedure.

If the advice given in the statements presented above is followed, it will quickly be discovered that this type of surgery is not too difficult. It is important, however, to operate with great care, so as not to disturb the blood supply of the tissues to be retained. It must be kept in mind that no matter how small the piece of remaining ovarian tissue is, it is well worth conserving.

The following authors are quoted because their papers likewise express the belief that it is not difficult to remove the cystic portions.

Dockerty,[8] of the Mayo Clinic, reviewing four hundred articles in the literature on the subject of ovarian neoplasms in general, states: "When such small dermoids are encountered they should be shelled out without rupture and the resulting raw surface apposed with a minimum of fine suture material. Pregnancy has occasionally ensued after such conservation of the ovarian tissue."

I believe that it is possible to extend these remarks by the statement that conservative surgery can also be practiced in cases with large dermoid cysts. The cysts in the cases described above were each nearly the size of an orange.

Meigs[9] writes that dermoid cysts may be treated by excision with the ovary or excision from the ovary. He also concludes his discussion of ovarian tumors by saying "The treatment of certain ovarian lesions is definite and may be conservative. . . ."

The following cases are included in this paper because they likewise help prove the value of conservative ovarian surgery. These were cases of endometriosis, reasonably well developed, in patients

who before operation had been considered incapable of bearing children.

J. P.,* a 22-year-old woman who had been married 1½ years, had been well up to 6 months prior to operation. During that time increasingly more painful menstrual periods had developed. On August 30, 1944, she was operated upon by me at the Cambridge Hospital. Owing to a chocolate cyst, the left ovary was nearly the size of a peach. The tube was intimately adherent to it. The uterus was in retroversion. The right tube appeared normal. The right ovary contained simple cysts. There were numerous endometrial implants over the surface of the bladder. A left salpingo-oophorectomy, incision of the cysts of the right ovary, excision of the endometriomas and uterine suspension were performed.

Pathological examination by Dr. MacMahon disclosed an endometrial cyst of the ovary, with endometriosis of the tube and of the adjacent serosal surface. The ectopic endometrial tissue was "in secretory phase" as was the endometrium.

In November, 1945, the patient's husband returned from military service. She became pregnant during January, 1946, and was delivered (because of disproportion) by low cervical cesarean section on November 2, 1946, of a healthy female baby weighing 7 pounds, 13 ounces. At this operation, the remaining right ovary was examined. It was normal in appearance.

This case also demonstrates the value of conservative ovarian surgery. It may seem that this point is being labored. If reiteration drives home a thought, it is well for the occasional operator, espepecially, to appreciate the value of conservatism. My belief is that this advice cannot be repeated too often and that the lives of many women, as well as their marital relations, can be saved from being wrecked by exceedingly small pieces of ovarian tissue. Greater caution must be exercised by the surgeon in his decision to remove one ovary even if the other is normal. In many cases, resection of a pathologic ovary leaves enough functioning tissue to give the patient two functioning ovaries against the possible future ravages of time.

The following case falls into a similar category.

G. M., a 26-year-old woman, had been married 5 years and had been unsuccessful in becoming pregnant. An extensive abdominal operation was performed by another surgeon in 1942. The patient was informed that part of an ovary had been removed during this operation. Subsequently, she continued to have severe pain during the menstrual periods. Examination in January, 1944, disclosed enlargement of the left ovary to nearly four or five times the normal size. On January 19, 1945, I performed lysis of intra-abdominal adhesions, a left salpingo-oophorectomy and partial resection and repair of the right ovary.

The left ovary was enlarged about four times the normal size, owing to "chocolate" contents. A presacral neurectomy and excision of multiple endometriomas were done. The right ovary contained a chocolate cyst, which was resected.

The pathological report† disclosed "chronic perisalpingitis and peri-oophoritis, and endometrial cysts of the ovary."

This patient was urged to try for pregnancy soon after her discharge from the hospital and on April 4th, she had her last regular menstrual period. On January 18, 1946, after a test of labor, this patient was delivered (x-ray measurements — diagnosis of disproportion), by low cervical cesarean section, of a normal, male baby, weighing 6 pounds, 6 ounces. At operation, the remaining right ovary was examined. It appeared normal.

*Cambridge Hospital S-44-1093.

†Leary Laboratory. P. 45-299.

Discussion

In these cases conservative ovarian surgery was practiced. The older textbooks invariably advise the complete removal of ovaries in such cases. If this advice had been followed in the cases described above, the patients would have lost completely the opportunity of becoming pregnant, would have suffered sudden surgical menopause and would also, as a result of these changes, have had difficulty in their domestic welfare.

Reference has been made to "older textbooks." As a matter of fact, even recent articles in the medical literature seldom allude to the use of conservative surgery. This paper, therefore, is written as a plea that the surgeon consider carefully his decision to remove ovaries, that he remember the dire consequences from the removal of both ovaries in young women, and that he preserve as much ovarian tissue as possible.

Summary

Four cases in which both ovaries were not removed, even though the tissues were pathologic, are cited.

Two cases of bilateral ovarian dermoid cysts are described. In both, dime-sized portions of tissue were preserved. One patient, who married later, was subsequently delivered of 3 normal children.

Two cases of endometriosis are reported, both with endometrial implants and involvement of both ovaries. In each, one ovary was removed. The remaining ovary was partially resected. Both patients were subsequently delivered of normal healthy babies and had regular painless periods after these deliveries.

In the treatment of a large number of women over a period of seventeen years, conservative surgery has been practiced in numerous cases, and the final results have been most gratifying.

The 4 cases described were chosen as the most suitable to drive home the point that conservative ovarian surgery is possible and ultimately pays large dividends to the patient.

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CLINICAL NOTE

THORACIC TENDERNESS IN PULMONARY INFARCTION

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DURING the last decade, steadily increasing attention has been paid to the early diagnosis, in both medical and surgical cases, of phlebothrombosis and thrombophlebitis. Earlier diagnosis and prompt treatment with the anticoagulants, or by venous ligation, have appreciably reduced the number of unfortunate cases in which the patient, making an uneventful convalescence, suddenly succumbs to a pulmonary embolism. However, in spite of routine daily examinations of the legs and scanning of the chart, the first evidence of such a process is all too often observed too late.

Boyd[1] divides pulmonary emboli into three classes: large emboli occluding a main artery and causing death with respiratory distress; medium-sized emboli producing physical signs of an infarct; and small emboli causing symptoms but not physical signs of infarction. It is the purpose of this communication to describe a physical sign that occurs in the small emboli in the third classification.

It is important to make the diagnosis of pulmonary infarction and institute treatment immediately after the episode has occurred, since there is no assurance that a second, and perhaps fatal, embolus will not occur at any time. Yet x-ray study cannot be expected to confirm the diagnosis for nearly twenty-four hours, and physical signs in the lungs are totally absent if the embolus is small and may be equivocal if it is present.

An early and striking finding in 4 well established cases of pulmonary infarction occurring postoperatively, and in 1 equivocal case occurring in an orthopedic patient, has been marked tenderness of the chest wall, approximately over the site of infarction. This tenderness in all cases was severe enough to cause the patient to cry out and flinch if moderate pressure were applied. It was present in 1 case as early as six hours after the initial onset of pleuritic pain and disappeared gradually in from forty-eight to seventy-two hours. The area of tenderness varied in diameter from 2.5 to 20 cm., presumably depending on the extent of the underlying pleuritis, and in each case a sharply demarcated point of maximum tenderness could be demonstrated in one of the intercostal spaces.

Brief abstracts of the pertinent data in 5 cases follow:

CASE 1. A 39-year-old housewife developed severe pleuritic pain in the right anterior portion of the chest 11 days after choledochostomy. The temperature rose to 100°F. Examination revealed exquisite tenderness in the right anterior portion of the chest with point tenderness in the sixth interspace in the anterior axillary line. The lungs were clear, and x-ray examination of the chest was negative. There was tenderness in the calves of both legs with a positive Homans sign on the left. A bilateral femoral ligation was performed.

CASE 2. A 20-year-old girl developed acute deep thrombophlebitis of the left leg on the 8th day after ileostomy for ulcerative colitis. This was treated by repeated paravertebral blocks, caudal blocks and heparin-dicoumarol anticoagulant therapy. On the 9th postoperative day, a mild pleuritic pain developed in the right anterior portion of the chest without other symptoms. Physical examination showed point tenderness in the sixth interspace in the anterior axillary line, but the lungs were clear and x-ray study of the chest was negative. On the following day a friction-rub was audible in the involved area.

CASE 3. Eight days after a cholecystectomy, a 53-year-old housewife developed pleuritic pain in the right posterior portion of the chest that was so mild that she did not mention it for 24 hours. There were no other symptoms. The temperature was 99°F., and the respirations 28. There was definite tenderness over the right lateral and posterior portions of the chest with point tenderness. There were suppressed breath sounds and moist rales in this area. X-ray study of the chest was interpreted as showing atelectasis. There was questionable tenderness over the left femoral vein. Anticoagulant therapy was instituted.

CASE 4. A 25-year-old man, scheduled for exploratory laparotomy, had operation delayed for 10 days pending evaluation of deep tenderness noted first in the right calf and later in the left calf. There was no elevation of vital signs, and Homans sign was negative. However, on the 1st postoperative day there was gross hemoptysis. On the 2nd postoperative day the patient noted severe pleuritic pain in the right anterior portion of the chest. There was extreme tenderness in this area. The temperature rose to 102°F., the pulse to 110, and the respirations to over 30. X-ray examination showed consolidation of the right lower lobe. Anticoagulant therapy was instituted.

CASE 5. A 73-year-old woman had been in bed 3½ months, after an open reduction and nailing of a fractured hip, when she developed a sharp pleuritic pain in the left anterior portion of the chest, which lasted for 3 days. There was point tenderness in the fifth interspace in the anterior axillary line, but physical examination was otherwise negative, with no signs of phlebothrombosis. X-ray study of the chest 3 days later was negative. No therapy was instituted, and no further episode occurred.

It is significant that in none of the cases did there appear the combination of symptoms and signs that are generally considered typical of pulmonary infarction — that is, cough, hemoptysis, pleuritic pain, fever, increased respiratory rate, distant bronchial breath sounds, moist rales and x-ray evidence of infarction. Two cases showed pleuritic pain and thoracic tenderness alone, whereas another had a transient friction rub in addition that could easily have been missed. Only 2 cases revealed changes in the lung by physical and x-ray examination.

It is also significant that in 1 case the diagnosis of pulmonary infarct was not considered during the hospital stay, and that in another, a delay of several hours ensued before the true nature of the episode was appreciated and ligation performed. In a third case the symptoms were so insignificant that the patient did not mention them until twenty-four hours had elapsed.

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The significance of this sign (thoracic tenderness), which is certainly neither new nor unknown, is apparently not widely appreciated. A survey of the standard textbooks of medicine and physical diagnosis, as well as various systems of medicine and texts on differential diagnosis, failed to elicit any reference to the sign. A review of the literature for the last ten years, however, resulted in the finding of one paper on the subject. McMillan,[2] in 1942, described extreme tenderness on light fist percussion over the affected area in cases of pulmonary infarction and reported 14 cases. He considered this sign of great value in the differentiation of pulmonary infarction and pneumonia.

It is suggested that the presence of chest tenderness in connection with a pleuritic type of pain in the absence of trauma be considered suggestive of pulmonary infarction, even in the absence of supporting symptoms, signs or x-ray changes, and that treatment be undertaken on that basis.

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MEDICAL PROGRESS

SYPHILIS

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AT THE time of this writing it is approximately four years since the publication of the first report on the use of penicillin in the treatment of syphilis.[1] The remarkable efficacy of this drug in combating man's most crippling venereal disease is attested by the fact that in so short a time it has become accepted as standard therapy for syphilis. A vast effort has been expended in widespread and well organized research projects, both experimental and clinical. From ten to twenty years are required to evaluate properly the therapeutic results of any approach to syphilis in all respects except immediate effects on fresh infections. The response of early syphilis to penicillin has been so dramatic, however, that the acceptance of this drug is now granted. Its long-term results will have to await further and prolonged observation periods. Despite this remarkable new weapon and the extraordinary success achieved by the military forces during the war, the trend of venereal-disease incidence is again on the rise.

Public Health

The advent of penicillin has resulted in an increase of the treatment of syphilis by physicians engaged in diverse types of practice. This antibiotic has simplified the treatment of syphilis to the point where it can be administered by most practicing physicians with a modicum of danger. Anyone except those in more remote specialties can treat the disease, provided their plan of therapy is adequate. Two main pitfalls enter into the problem at this point. With such increased ease of therapy, a natural hazard is the possibility of treatment without accurate diagnosis. Cases of this sort have come to the attention of most syphilologists in which physicians with undoubted skill in their own fields of work have too readily assumed the diagnosis of syphilis and instituted treatnent. There are few diseases with more sociologic import than syphilis, and one should exert extreme care in making the diagnosis, entirely aside from the medical implications. Syphilologists, more than other physicians, are extremely loath to make a diagnosis of syphilis without unequivocal evidence; this applies particularly to the primary and secondary stages of the disease. The second and possibly even greater hazard in the treatment of syphilis by physicians in general practice is the likelihood of employing insufficient dosage of penicillin. There are many facets to this problem that have not been worked out satisfactorily, and programs of therapy are still constantly being changed. Penicillin causes so comparatively few reactions that overdosage is far less hazardous than with any other treatment for syphilis. Consequently, it is better to err on the side of giving more penicillin than is thought necessary, rather than using insufficient quantities. This will obviate the likelihood of infectious relapse that might easily go unrecognized until many more persons had been infected. It should not only increase the percentage of immediate "cures" but also go far toward preventing the late serious crippling sequelae of syphilis. The economic burden already entailed by syphilitic inmates of mental institutions is far too great. During the decade 1935–1944, inclusive, first admissions to mental hospitals in the United States due to neurosyphilis of all varieties comprised a ratio of 6.7 per 100,000 population, exclusive of the armed forces overseas.[2]

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Statistical Trend

The remarkable accomplishment of the military forces during the war in keeping the incidence of venereal disease lower than any previous wartime rate in history is well known. A survey of venereal diseases among the civilian population during the same period shows a trend that is not so encouraging.[3] The cases of syphilis diagnosed in the states and territories during the years 1941–1947, inclusive, and excluding all military sources, reveal a different state of affairs. During the first two years of the war, cases of syphilis reported for the first time among civilians increased steadily to a maximum of 576,000 in 1943. For the next two years, there was a significant drop, a low of 368,000 cases being reached in 1945. An increase of about 0.5 per cent, which was not significant, took place in 1946, and one of somewhat over 5 per cent was reported for the first half of 1947, which is a strong indication for the need of more urgent control measures. The majority of this elevation in rate took place in primary and secondary cases, pointing to the existence of reservoirs of readily available fresh disease. When further broken down, the statistics show a steady decrease in the number of late, late latent and congenital cases of syphilis during the same period of six years. These figures reflect the effectiveness of control measures that were carried out by both the armed forces and the United States Public Health Service. This downward trend in late crippling disease and congenital infections will not be maintained if the incidence of fresh infections continues to rise.

A purely military survey indicates a similar but more pronounced trend.[4] The report shows that a distinct increase in venereal disease became evident in the navy soon after VJ Day. This was reflected in all naval districts and made venereal disease the outstanding factor in morbidity at that time. The most marked increase was apparent in noncontinental areas and ships; in continental naval districts the increase was equally consistent, though slower. Naval personnel in the West Pacific area sustained the greatest increase of venereal disease, the rise in rate multiplying more than elevenfold in one year. Although military personnel has been drastically reduced since the war, there has been no relaxation in the attempt to control venereal disease in that quarter. A working agreement has been reached between the Army, Navy, Coast Guard, Federal Security Agency and American Social Hygiene Association, establishing peacetime relations in venereal-disease control.[5] In addition to the maintenance of military measures, this includes procedures by all public-health departments directed toward case finding, diagnosis, treatment and repression of sources of infection among the civilian population. The armed forces will continue to declare "out-of-bounds" establishments that serve as places of pickup. The United States Public Health Service will continue to assist and co-operate with public institutions and scientists in the conduct of research and experiments relating to diagnosis, treatment and control of venereal disease.

There has been an impression that in recent years syphilitic infections among the teen-age groups have constituted an increasing proportion of the problem of venereal-disease control. It has also been thought that the vast numbers of men in military service who were concentrated in encampments had a pronounced influence on venereal-disease rates. An analysis of statistical data concerning patients admitted to public clinics for early syphilis from 1941 through 1944 contradicts these impressions.[6] The analysis was limited to females and indicated that a shift into the teen ages has not been nationwide and that a tendency toward an earlier age of infection among white females was most pronounced in the presence of an increasing civilian population, particularly in areas of war-boom industrial concentration. Increasing military populations seemed to have little or no tendency to be associated with an increased proportion of teen-age infection among white females, presumably because of active control measures within the armed forces.

Control Measures

There are many communications giving evidence of the awareness of public-health authorities of the increased menace of syphilis. Information regarding sources of infection has always been difficult to obtain. Self-interview forms have been devised to elicit information from reticent patients.[7] These forms include pertinent advice regarding the danger and infectiousness of venereal disease and thereafter request information regarding sex partners, but do not require the patient to sign his name. The information is thus confidential, and co-operation is sometimes more readily obtained. Studies of epidemiologic activity on syphilis contacts reveal that approach by telegram, by visits to the patient and by letter all have their value in persuading suspects to report for examination.[8–10] Telegrams sometimes have a surprisingly effective result and may be even more efficient than a direct personal visit. Registered mail is obviously more impressive than ordinary letters. Personal visits take time and are expensive and comparatively slow, both in finding contacts and in returning patients to treatment. Compulsion is an effective but also an expensive method of case holding and cannot be used until a considerable time has elapsed since the patient's last treatment. Telegrams and registered letters are to a large extent effective in solving these problems. Compulsory attendance for an examination, for treatment or for those who have permitted therapy to lapse should be avoided if

possible. Co-operation is not obtained by compulsion, and compulsion should be used only as a last resort.

Postgraduate instruction in venereal-disease management is available in almost every medical center of the country. Postgraduate refresher courses are being organized throughout practically every state. The practicing physician and public-health officer should be brought up to date regarding new methods of treatment and recent refinements in the diagnosis of venereal disease. Diagnostic and consultation services are available to physicians in nearly every community through clinics, medical schools and public-health agencies. Training or refresher instruction can be obtained either on an individual or a group basis, and if practicing physicians avail themselves of these opportunities many unfortunate errors can be avoided; simultaneously, an increased efficacy of venereal-disease control can be attained.

The importance of nurses in venereal-disease control is being more properly emphasized. The value of a nurse as a case finder cannot be overestimated.[11] An alert nurse in clinic, school, industry or on visiting-nurse duty can find many opportunities in her daily routine to serve as a case finder. Patients will sometimes more readily confide in a nurse than a physician and with proper interviewing may reveal contacts that would otherwise be undiscovered. The industrial nurse's responsibilities in venereal-disease control have increased since the end of the war.[12] The interests of management and labor in a good educational program are being stimulated. The industrial nurse fits neatly into this program both from the educational standpoint and in assisting case-finding measures. She has many opportunities for personal counseling with employees in family health problems and can include many phases of venereal-disease control. In a large clinic the nurses are responsible to a great extent for the atmosphere of the clinic and are an important factor in obtaining the co-operation of the patients.[13] The nurse may serve as a liaison between the doctor and the patient and between the patient and his family when trouble arises. She can often explain to the patient the physician's recommendation for the need for treatment of himself as well as contacts. Nurses may have more tact and ingenuity than physicians in many instances. Their responsibility in the education of the patient is of great importance. This is especially true of the public-health nurse in rapid-treatment centers, where the nurse is of inestimable value.[14]

Morbidity and Mortality

Among 3970 autopsies performed at the Yale University School of Medicine between 1917 and 1941, 380 showed evidence of syphilitic infection.[15] Of these patients 198 (52.1 per cent) had never received treatment. Anatomic lesions of syphilis were found in 77 (38.9 per cent) of these untreated patients, but in only 46 (23.2 per cent) was death considered to have been due primarily to syphilis. One hundred and twenty-one patients revealed an absence of anatomic lesions of syphilis, and in 35 cases the serologic tests for syphilis were negative during the last hospital stay. The 77 untreated patients with post-mortem changes revealed 88 cardiovascular lesions, 8 lesions of the central nervous system and 10 other types of lesions. These results closely agree with the observations of Bruusgaard,[16] who was the first to report an authoritative series of untreated patients examined pathologically years later. The current report is an important study, and it should be read in the original by all syphilologists.

A survey by the Bureau of the Census of vital-statistics rates in the United States reveals a steady decline in the death rate from syphilis from 1938 to date.[17] There has surely been no de-emphasis of syphilis as a cause of death nor any decrease in the ability of doctors to recognize it during this time. Therefore, it is believed that this decline is a real one that can be attributed to the venereal-disease-control program. Evidently the treatment schedules advocated in the last few decades have been to good effect. As might be expected, the decrease in infant mortality due to syphilis has been even more pronounced. A survey of the most recent communications on the mortality of syphilis has given rise to formulation of a policy regarding the eligibility of syphilitic persons for life insurance.[18] This study and its recommendations regarding eligibility for insurance have been carried out by eminent syphilologists rather than the usual actuarial approach of insurance companies. It is of primary value and interest to the insurance actuarians but contains information valuable to anyone dealing with syphilis. The various types of the disease are classified regarding insurability, adequacy of treatment and probationary periods required after treatment before insurance should be granted.

Experimental Studies

Penicillin in Oils

Although penicillin in peanut oil and beeswax has been under study for some time, a recent report indicates that it may not be the best combination for delaying absorption of the antibiotic.[19] Injections of calcium penicillin of high potency suspended in hydrogenated cottonseed oil were found to maintain a penicillin level of 0.1 unit per cubic centimeter of blood for at least six hours in 80 per cent of cases, whereas in the beeswax-peanut-oil mixture it maintained that level in only 66 per cent. Hydrogenated oil delayed the absorption of penicillin more than the plain oils in all the various diluents tested. Undoubtedly, a good deal more work must be done along these lines before the best preparation is ultimately identified.

In experimental syphilis in rabbits, the effect of penicillin in peanut oil and beeswax has been compared with penicillin administered in isotonic solution of sodium chloride.[20] The oil-wax suspension was definitely more therapeutically effective in the treatment of syphilitic orchitis of rabbits. When a single minimum curative dose of penicillin was employed, the oil-wax suspension was approximately ten times more efficient. When a single daily intramuscular injection was used for eight days in succession, the oil-wax suspension of penicillin required a minimal curative dose approximately one fifth as large as the saline solution. This work has been confirmed by other observers, who obtained essentially comparable figures.[21] The curative dose of penicillin, whether in aqueous solution or oily suspension, varied with the number of injections into which treatment was divided. Penicillin in aqueous solution had to be subdivided into two to fourteen times as many injections as the oil-beeswax suspension to be equally effective. The superiority of the oil and wax suspension was particularly striking in schedules involving relatively large injections. The smaller the individual dose of penicillin, the less pronounced was that margin of superiority.

Penicillin and Adjuvant Measures

A large number of combinations of penicillin with heavy metals, arsenic, hyperpyrexia and other measures have been undergoing experimentation. The use of penicillin and bismuth in the treatment of experimental syphilis of rabbits has been found highly effective and safe with a minimum of reaction.[22] A fat-soluble preparation of penicillin in the form of methyl ester was employed in the same fashion and seemed even more effective in its combination with bismuth; syphilis in rabbits required lower doses for cure, and the method was then applied to human beings, with equally satisfactory results.[23] Prolonged periods of observation will be necessary in all these studies to ascertain long-term effectiveness. Confirmation of the value of combined therapy was not long in appearing, however, and the use of oxophenarsine hydrochloride combined with penicillin was likewise found of considerable value.[24] A different type of bismuth salt was employed with just as satisfactory results. Oxophenarsine hydrochloride by both intravenous and intramuscular injection showed decided synergistic or adjuvant therapeutic effects in the penicillin treatment of syphilitic orchitis of rabbits. Bismuth subsalicylate is the most common salt of that metal to be employed in the treatment of syphilis. Its toxicity and therapeutic efficiency have recently been compared with those of two other bismuth compounds.[25] The three bismuth compounds proved similar in therapeutic efficacy with generous margins of safety. There is therefore no indication for the departure from general usage of the bismuth salicylate suspended in oil. All three types of bismuth preparations studied were mol for mol from one half to two thirds as active as Mapharsen in the treatment of experimental syphilis of rabbits. The margin of safety for the oily suspension of the subsalicylate was between six and eight times greater than that between effective and toxic levels of Mapharsen.

A new drug, Caronamide, is now being studied with the purpose of increasing penicillin plasma concentrations in man.[26] This substance, when given orally to patients receiving penicillin, produced a physiologic and reversible inhibition of the excretion of this antibiotic, which increased the concentration of the penicillin in the plasma. Although there is not yet general agreement whether the maintenance of a constant level of penicillin plasma concentration is more desirable than the attainment of intermittent high levels, there is at least a need for high concentration of penicillin at certain times. Caronamide, when administered orally, elevates the penicillin plasma concentration from two to seven times, after either the oral or parenteral administration of penicillin, and should have great therapeutic usefulness in the treatment of conditions that require high penicillin blood levels. It is now being applied to the therapy of patients. Extensive laboratory investigation of the physiologic, pharmacologic, toxicologic and bacteriologic properties of Caronamide have justified its clinical use. The action of this drug is to inhibit the elimination of penicillin at the level of the renal tubules. The effectiveness of Caronamide is said to depend on a "substrate competition between penicillin, which is excreted by the tubules, and Caronamide, which is essentially refractory to excretion by that transport mechanism."

The therapeutic efficacy of penicillin in vitro has been shown to increase with temperature.[27] Many syphilologists have been utilizing this fact in the combined treatment of neurosyphilis with penicillin and hyperpyrexia. A report has now appeared regarding the laboratory confirmation of this fact in experimental infections in rabbits.[28] In the treatment of early syphilis in rabbits the therapeutic action of penicillin was strikingly enhanced by a simultaneous increase in body temperature, evidenced by the fact that the effective dose of penicillin was thereby reduced to one tenth of its usual level. The combination of fever with penicillin is neither feasible nor desirable, however, for the treatment of early syphilis in man. Penicillin therapy may be supplemented by bismuth or Mapharsen, which do not carry the risk of fever therapy and require considerably less expenditure of time and money. In neurosyphilis, however, the situation is quite different: penicillin alone may not suffice, and the

advantages of fever therapy are already well recognized. Whether the hyperpyrexia exerts its own effect or serves also to enhance the spirocheticidal activity of penicillin, their use in combination should yield results exceeding those hitherto obtainable.

Experimental Reinfection

The question of reinfection vs. relapse has been a most controversial one since the advent of penicillin with its rapid eradication of lesions and apparent "cure" of early syphilis. Recurring evidence of clinically active disease after penicillin therapy has been variously interpreted as relapse or reinfection, depending upon the observers' evaluation of the history and symptoms. A relapse might thus be a treatment failure. On the other hand a reinfection could be used as a criterion of cure, or possibly of superinfection. A study of experimental syphilis in the rabbit has been conducted to determine what incidence of reinfection could be produced within ten days of the completion of adequate penicillin therapy.[29] Acute syphilis in rabbits was cured in three days with penicillin therapy; reinoculation was then attempted ten days after treatment had been completed. Twenty-seven per cent developed dark-field-positive chancres at the sight of reinoculation, and the remaining 73 per cent developed a symptomless infection confirmed by positive lymph-node transfer. Untreated rabbits with acute syphilis, reinoculated with a homologous strain of spirochetes at the same time period as the treated animals, did not develop clinical evidence of reinfection. It appears from this experiment (in which the second inoculation was introduced before the initial lesions had completely healed) that symptomatic or symptomless reinfection may take place before the disappearance of either the original clinical symptoms or the seropositivity of the host. This explains the so-called "ping-pong" syphilis, which has been noted in some patients with early syphilis treated with penicillin, in which a repeated interchange of infection occurs between two people with the same strain of *Treponema pallidum* (*Spirochaeta pallida*). The human body does not have time to produce a tissue immunity when the infection is eradicated so quickly. A symptomless reinfection may occur with a clinical and laboratory pattern resembling one of true serologic relapse in untreated animals or human beings. There is at least an immunity that lasts for a varying period and prevents reinfection in untreated cases.

Penicillin Resistance

It has been suspected that penicillin-resistant strains of *Tr. pallidum* might appear. Earlier work with repeated culture passages through mediums containing substerilizing concentrations of penicillin did not show evidence of increased resistance to penicillin.[30] Further experimental evidence has now appeared from work with syphilis in rabbits.[31] There was no evidence that *Tr. pallidum* acquired any resistance to penicillin after three consecutive passages through the testicles of rabbits treated with subcurative amounts of commercial penicillin. After the final passage the last group of rabbits was given a minimal curative dose of penicillin, and total cure was confirmed by lymph-node transfer. If this is true of the human disease it is exceedingly encouraging, since up to now almost every chemotherapeutic or antibiotic approach to human infection of any sort has sooner or later encountered resistant strains of organisms, regardless of the infection.

Synthetic Penicillin

The complexity of processes required for the production of penicillin naturally led to attempts at synthetic development of this antibiotic. Synthetic penicillins have been produced independently in the United States and Great Britain as long ago as 1944.[32] Because of the obscurity of reaction mechanism, the synthesis at the present stage of development cannot be used as proof of the structure of penicillin. Improvement in the methods of synthesis have not progressed sufficiently to make commercial production practicable. It may be possible, however, to make new penicillins, which might possess even more desirable therapeutic properties.

Streptomycin

With the advent of another wonder drug, streptomycin, it was natural to expect quick investigation of its possible effect on syphilis. It was found that the smallest amounts of streptomycin that cured syphilis in rabbits were more than three thousand times greater than the quantity of penicillin G required for effective sterilization of the infection.[33] The use of streptomycin for syphilis is obviously impracticable. Subsequent study of the same problem by other investigators was even less encouraging.[34] Still further work pointed to the possibility that streptomycin has no actual effect on syphilis.[35]

Prophylaxis

In spite of education, various public-health attempts at control measures and new effective methods of therapy, the vagaries of human nature will probably always leave a place for prophylactic measures in the prevention of syphilis. The latest attempts to create effective prophylactic measures have been concerned with the use of propylene glycol solutions and ointments of various arsenox-

ides.[36] Aqueous solutions in dilute soap were also employed. All these preparations had an encouraging prophylactic effect in preventing syphilis in rabbits, the ointments being the least useful regardless of the type of base employed. When infection was attempted through normal skin the soap solutions were highly effective prophylactic agents. If direct access was provided to the blood or lymph channels, all the prophylactic measures were largely ineffective. The application of these principles to the prophylaxis of the disease in men would encounter so many variables that an assay of their value would be exceedingly difficult. The length of time during which the organism might remain accessible to the prophylactic drug is unknown. The infectiousness of the exposure would vary. The time interval between the exposure and the use of prophylaxis, as well as the skill of the prophylactic application, would make the results of dubious significance.

Staining Method

Numerous methods of staining *Tr. pallidum* have been reported in the past, but most of these require technics that are not readily available and often too complicated for convenient use. A reasonably quick staining method that may be more generally applicable has been described.[37] The entire process is said to take only one minute, but the description will not be repeated here. Its usefulness is somewhat limited since dark-field examination is generally available and is usually more reliable. In some cases in which exudate is profuse and relatively uncontaminated serum cannot be obtained, staining methods would be of use.

Immunity in Syphilis

Human beings do not possess natural resistance to syphilis, but some degree of immunity develops in man as a result of syphilitic infection. The mechanism of the defense process is still unknown. It is probably a tissue or cellular reaction, since the existence of humoral antibodies against syphilis have not been demonstrated. Numerous attempts to induce active or passive immunization against syphilis in man and animals have failed to produce any significant results. The relation of the positive serologic reaction to the organism's capacity to produce antibodies against spirochetes is not clear. Immunity at any stage of the disease is never absolute, but only relative. Untreated infection with syphilis confers on the human being immunity that prevents natural superinfection but does not protect him against massive artificial superinfection. Intensive treatment of early syphilis is in all probability capable of curing the disease. Such treatment abolishes all immunity that is in the process of development but does not endanger the patient if it is strong enough to eradicate the infection completely. Inadequate antisyphilitic therapy will seriously impair the natural defensive mechanism, and the patient will be left both without a cure and without defense. This often leads to neurorecurrences, therapy-resistant relapses and precocious tertiarism. One student of the problem believes that animals treated in the late stages are biologically cured and at the same time actively immunized because they were thoroughly infected for a sufficiently long time.[38] A patient might thus be completely cured and yet remain refractory to natural reinfection. The reinoculation test (reinfection) is not believed by others to constitute a reliable criterion of cure in treated animals.[39] A symptomless infection is held to be possible in these animals, and this could be determined only by removal of tissue from treated animals at appropriate intervals after cessation of treatment and inoculation of that tissue into normal animals. These writers further believe that immunity is a special form of allergic hypersensitiveness. It is claimed that the whole course of untreated syphilis can be explained on the basis of allergy. The chancre is thus regarded as an allergic defensive measure that marks the beginning of the organism's altered reactivity to reinfection. The cutaneous manifestations of secondary syphilis are also thought to be manifestations of an allergic defense mechanism. The tertiary stage of the disease frequently shows severe local manifestations, during a phase in which the number of spirochetes is small, and these events are regarded as signs of a high degree of allergy. It is possible that a new approach toward understanding the nature of immunity in syphilis will be possible if further study confirms the preliminary demonstration of complete sterilization by penicillin therapy of animals experimentally infected with syphilis.[29]

A study of the same problem in infected rabbits treated after periods of three or four months with arsenobenzol injections led to the conclusion that immunity cannot depend on the persistence of parasites but must be an acquired one that developed at least three months prior to the treatment.[40] Attempts at reinoculation, as well as tissue inoculations from the treated animals, were confirmatory. Only 3 per cent of the reinoculated animals developed clinical syphilis, and 6 per cent presented symptomless reinfection. It was further shown that the immunity persisted in varying degrees for approximately a year before it decreased appreciably. Still another author proposes the term "reactivation" for infections such as syphilis, in which an "immuno-allergy potential" is all that remains of an infection and in which reinoculation does not produce reinfection or superinfection.[41] He believes that parts of the syphilitic process may be evoked by superinoculation in such cases, because the first course of events in an infection cannot be exactly repro-

duced while some degree of allergic state or immunity persists. It is further stated that in absolute cure neither spirochetes nor potential remain.

It is obvious that thorough disagreement if not confusion exists rather generally regarding the problem of immunity in syphilis. Perhaps the best lesson to be learned from this discourse is the fact that a small amount of treatment in early syphilis, which is inadequate to eradicate the infection, is worse than none. It will interfere with the body's own defensive mechanism, fail to eliminate the infection and leave the patient worse off than nature alone would have left him. Perhaps his untreated infection will be discovered at some later date during the so-called "hyposensitive phase," when it may be at least arrested by therapy, before he reaches the hypersensitive or allergic state in which the explosive tertiary tissue reactions take place.

(To be continued)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 34031

PRESENTATION OF CASE

First admission. An eighteen-year-old girl was admitted to the hospital with dyspnea.

Three years previously, following the death of her mother with pulmonary tuberculosis, she became run-down and developed cough, sputum and hemoptysis. An x-ray film showed cavitation in the right apex, and she was hospitalized in a sanatorium for two years. While she was at the sanatorium a good collapse was obtained by pneumothorax, and she gained weight and became symptom free. The pneumothorax was continued at intervals after discharge. Three months before admission, following a refill of air, she developed a persistent dry cough, fever and night sweats.

Physical examination revealed a well developed, well nourished girl with signs of fluid in the right side of the chest.

The temperature was 99 to 100°F., the pulse 90, and the respirations 20.

Examination of the blood and urine was negative. An x-ray examination of the chest showed a pneumothorax on the right, the fluid level lying opposite the seventh interspace posteriorly. The right lung was about three quarters collapsed, and no cavities were seen. The left lung field was clear. The heart was not displaced.

A chest tap yielded purulent fluid. Ordinary aerobic and anaerobic cultures were negative; a guinea-pig inoculation was positive for tuberculosis.

The temperature and pulse subsided, and the patient was discharged eight days after admission. Pneumothorax was permanently discontinued.

Final admission (nine years later). The patient was readmitted because of dyspnea.

For many years she had felt well. She had married and had had a normal pregnancy. Two years before readmission she developed a lump in the right breast. A simple mastectomy was done at an outside hospital, and the pathological report was carcinoma (Grade II). She then received fourteen radium treatments. Six months later she noted a lump in the right axilla, and a complete axillary dissection was done. She made a good recovery and worked as a cook until four months before re-entry. At that time she began to have pleuritic pains in the bases of the lungs and shoulders, shifting from one side to the other, associated with a temperature of 100°F., cough with some expectoration of white material, anorexia, nausea and vomiting and weight loss. In the past month there was also rapidly progressive dyspnea, weakness, dizziness and a temperature of 98 to 101°F.

Physical examination revealed a well nourished, orthopneic woman. There were flatness and absent breath sounds in the lower half of the right side of the chest.

The temperature was 99°F., the pulse 110, and the respirations 20. The blood pressure was 134 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 11.5 gm. and a white-cell count of 12,800, with 89 per cent neutrophils. The urine and stools were normal. A Congo red test showed 60 per cent retention of the dye in one hour.

An x-ray film of the chest showed the right lung expanded to only half the thoracic cage and covered by a thick layer of organized pleural exudate (Fig. 1). Fluid and air filled the remaining portion of the chest cavity, the fluid level being at the ninth rib posteriorly. There was also considerable thickening of the parietal pleura. It seemed that only the upper lobe of the lung contained air, the remaining portion of the lung being drowned. The mediastinum was not displaced. The left lung was clear.

A thoracentesis was done, and 300 cc. of thick, turbid fluid was removed. Ten days later the fluid had reaccumulated, and another 200 cc. was removed. Ordinary cultures of this fluid showed no growth. Two weeks later the patient complained of a constant aching epigastric and left-upper-quadrant pain unrelated to food. Nausea and vomiting became more frequent. A large, poorly defined epigastric mass was palpated. A peritoneoscopy was unsuccessful because of omental adhesions to the liver. This operation was followed by subcutaneous emphysema and persistent drainage of ascitic fluid through the opening. A plain film of the abdomen showed little, if any, air in the peritoneal cavity, most of it being distributed through the various layers of the anterior abdominal wall. The soft-tissue contours of the belly were obscured. A gastrointestinal series showed a normal esophagus. The stomach was displaced anteriorly and to the left by an epigastric mass, which was in the position of the left lobe of the liver. No evidence of intrinsic disease of the stomach or duodenum was found. Three weeks later there was pain low in the back, radiating down both legs.

The patient lost ground rapidly. Prior to death she was slightly icteric and had a miliary pustular purpuric rash over the upper limbs and shoulders. She died five weeks after readmission.

Differential Diagnosis

Dr. Donald S. King: This is the story of a woman of twenty-seven who had a wasting disease of four months' duration, and this disease ran a febrile course. On physical examination there were two important findings: pleural effusion on the right and an epigastric mass. There was a history of two wasting diseases — tuberculous empyema and possibly generalized tuberculosis, and cancer of the breast with possible metastases. Both diseases can cause pleural effusion and abdominal fluid.

Did she have tuberculosis? Did she have cancer? Did she have both? One has to examine the three parts of the story. First, let us take the course of the disease. I stress the fact that it was a febrile course, and I consider that fact important. Very often when one follows the cases of known metastatic carcinoma from the breast with pleural effusion, temperature enters the picture and we wonder whether we are dealing with infection and not with a growth, but I do not believe that a persistent temperature for four months, as I assume this to have been, is quite consistent with cancer alone. To my mind, however, the febrile course favors tuberculosis. At the end pain occurred in the back and was referred down the sciatic nerve, but I think that it is too late to call that definite spinal metastases from the breast, although that is a common complication with such cancer. The slight icterus at the end and the miliary purpuric lesions on the shoulders, I think, can be explained on either basis, perhaps slightly better as tuberculosis than cancer, but they are of no great significance.

Dr. Tracy B. Mallory: Dr. King, would you like to see the temperature chart?

Dr. King: Certainly. It seems that the patient was running only a slight temperature. She came in with a temperature of 101°F. Following that it was almost always above 99°F., occasionally 100. At the end the rectal temperature was 99 to 100°F., and finally she had a temperature of 104°F. This does not support my thesis too well. It was not a really febrile disease. I expected the chart to show a swing from 99 to 101°F. But I still think that the fever is a little more consistent with tuberculosis than with cancer.

There are two points about the pleural effusion. In the first place, the fluid is described as definitely thick and turbid, and a thick, turbid fluid is the fluid of tuberculosis and not the fluid of cancer with metastases to the pleura. I do not remember ever having seen anything except a fairly thin, straw-colored or bloody fluid with cancer of the breast involving the pleura. There is no report of guinea-pig inoculation at that time. It was nine years previously that the patient was known to have definite tuberculous empyema. At that time the pneumothorax, which she had been carrying for three years, was discontinued. We do not know how many times the chest was tapped after that, and we do not know whether the lung re-expanded. We assume that it did. We dread the tuberculous empyemas, which may come with artificial pneumothorax, and that is one of the reasons why at present there is a slight tendency away from artificial pneumothorax treatment. This girl had had it nine years previously, and it looks as if she developed tuberculous empyema again.

May we see the x-ray films?

Dr. Stanley M. Wyman: The fluid level is probably intrapleural, as the record says. There is considerable collapse of the right upper lobe. The right lower lobe cannot be identified. It is probably almost completely collapsed. The right breast is missing. I do not see any metastases, and I do not see any evidence of hilar or mediastinal nodes. This is the film taken after the first tap. It shows that the fluid level has decreased. There is a thin rind over the lung and along the wall of the thoracic cage.

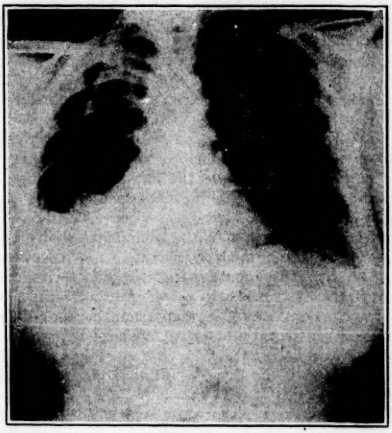

Figure 1.

Dr. King: There is no description of the film taken before the chest was tapped. After the tap the patient had a small bubble of pleural air. Where the pleural air was coming from after nine years is hard to say. She may have developed a bronchial fistula, following which she again developed tuberculous empyema. So far as this film is concerned, it does not offer much to differentiate tuberculosis and cancer, except that I can explain the pocket of air better on the basis of tuberculosis with bronchial fistula than by cancer with pleural metastases. After she had been tapped the pleura presented a

different appearance. I am interested in the terminology. Dr. Wyman called this a "rind," by which he means the thick layer of pleural exudate, which would have been called a "thickened pleura" five years ago. During the war Dr. Wyman saw the surgeons "peel" off these exudates and leave a rather shiny pleura beneath. Later there may be organization of the pleural exudate and a condition more like a real "thickened pleura." In any case I think that the x-ray appearance of the pleura, both visceral and parietal, is more consistent with tuberculosis than with pleural metastases from cancer. The patient was a good candidate for metastases to the pleura, and extensive pleural thickening may be the result in such cases, but so far as the clinical course and the x-ray film of the chest are concerned, I am still in favor of tuberculosis.

The third point for consideration is the epigastric mass. In the x-ray report this is described as an ill defined shadow displacing the stomach anteriorly and to the left.

DR. WYMAN: I assume that the location anteriorly was determined by the fluoroscopist. The stomach is certainly displaced to the left on both films. I cannot outline the definite mass on the film, and I cannot outline the abdominal viscera well because of the overlying gas in the abdominal wall. The gas is best seen in the lateral view.

DR. KING: I suppose that during the peritoneoscopy they pumped air as they usually do and pumped it outside rather than inside, because of the extensive omental adhesions. At least we are told that there were adhesions. I do not believe that this shadow is the liver, but I want you to tell me what it is.

DR. WYMAN: I cannot say that it is not the liver. I am rather inclined to think that it may be a slender tongue of liver tissue. The diaphragm is not elevated.

DR. KING: I would like to attach this shadow to this one here and call them both liver. Is that possible?

DR. WYMAN: It is hard to say that it is not.

DR. KING: You do not help me much. The mass is in the position of the liver. Both lobes may be enlarged. All we know is that there were omental adhesions around the liver, and a mass. If we accept the diagnosis of tuberculosis, a mass involving a good many retroperitoneal lymph nodes is a good possibility. After peritoneoscopy fluid drained out through the peritoneoscopic wound. On this account I think that I should incline again toward tuberculosis, rather than cancer. Ascitic fluid can certainly develop with cancer because cancer of the breast often metastasizes to the peritoneum and there is drainage through the peritoneoscopy tap or puncture holes. But the evidence seems better for tuberculosis than cancer. I am still on the fence in deciding whether the mass was the liver.

There are two or three things that I might mention in closing. Amyloid disease may come into this liver problem. Amyloid disease was obviously under consideration when the Congo red test was performed. The test in this case was, in my opinion, normal. I recently heard Amberson, of New York, say that unless 100 per cent of the Congo red is absorbed from the blood by amyloid tissue, the test is of no value. That is a strong statement, but I think that it is probably true in this case that the test was not positive. If this had been a large amyloid liver I think that it would have absorbed more than 40 per cent from the blood serum. Dr. Reuben Schulz, who has had a great deal of experience with amyloid disease, states that 20 per cent of all patients with tuberculosis autopsied at Middlesex County Sanatorium show amyloid disease. At Lakeville, where there is more extrapulmonary tuberculosis with osteomyelitis and so forth, the percentage is much higher. I have not seen a case for a year and a half. If this woman had tuberculous empyema for nine years she must have been a good candidate for amyloid disease. But I do not believe that we have evidence for tuberculous empyema over that period. Finally, if I make this diagnosis of tuberculosis, I am obviously on the spot regarding tuberculosis in the lungs. There is nothing that I can see in either of these chest films that looks like tuberculosis. The lower lobe that is mentioned as being "drowned," I do not believe is a drowned lobe in the sense that one ordinarily uses the term — that is, bronchial obstruction with infection beyond the obstruction. It is more to my mind an atelectatic lobe. What do you say, Dr. Wyman?

DR. WYMAN: I agree.

DR. KING: I shall have to make a diagnosis of generalized tuberculosis, for I do not believe that tuberculosis of the pleura alone caused the death. It must have spread beyond the pleura to involve the bronchi and probably the mediastinal and retroperitoneal lymph nodes. In spite of the x-ray film, I believe that there was bilateral pulmonary tuberculosis. Did the patient also have cancer? I am voting against it. There is no proof. I think that she was a good candidate for neoplasm, and I am willing to admit that there are all kinds of loopholes. Out in Denver recently I saw a note on the wall of the clinical amphitheater saying, "A man learns 10 per cent of what he hears, 30 per cent of what he reads, 50 per cent of what he sees, and 90 per cent of what he does." I am going to add that he learns 100 per cent of what he does wrong in these clinicopathological conferences.

DR. WYMAN: I should like to go on record a little more clearly regarding the liver. I believe that it may have been enlarged.

DR. KING: That does not to my mind make the diagnosis of cancer. Dr. Amberson also says that he found a good many fatty livers along with amyloid disease. Is it true, Dr. Mallory, that an en-

larged liver in amyloid disease is due to fat and not amyloid?

DR. MALLORY: I have not seen it often, but I imagine that it might occasionally be true.

DR. REED HARWOOD: The patient had icterus.

DR. KING: Yes; at the end she had slight icterus. I do not know how much stress to put on it. If one goes down the list of findings and symptoms in generalized tuberculosis it includes icterus. But it would not help in differentiation of the two.

CLINICAL DIAGNOSES

Metastatic carcinoma.
Tuberculous empyema.

DR. KING'S DIAGNOSES

Pulmonary tuberculosis.
Tuberculous empyema.
Generalized tuberculosis involving mediastinal and retroperitoneal lymph nodes.

ANATOMICAL DIAGNOSES

(Carcinoma of breast.)
Metastases to lungs, liver, axillary, mediastinal and retroperitoneal lymph nodes, ovary and vertebras.
Chylous ascites and hydrothorax, right.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Autopsy showed widespread metastatic carcinoma. That may or may not be the the entire answer. The liver was very much enlarged and full of metastatic carcinoma. There was also a very diffuse involvement of the lymph nodes of the mediastinum and up and down the aorta and retroperitoneal area, probably including the area of drainage of the thoracic duct. At the time of autopsy there was turbid fluid in both the abdomen and the cavity in the right side of the chest. Our impression of that fluid was that it was pseudochylous rather than purulent. There were very few cells found. At the time of death a guinea-pig inoculation of the pleural fluid had not been reported. Therefore, we did not include it in the abstract. This morning we sacrificed the animals, and they were entirely normal. On the other hand the cavity in the right pleura was encapsulated with thick, almost acellular collagen, which was in turn lined with a cheesy type of exudate. We were not able to demonstrate any microorganisms on smears. There was no suggestion histologically of active tuberculosis anywhere in the body. I think that the origin of the cavity was unquestionably a tuberculous empyema. The recent cavitation, however, was probably a mechanical phenomenon associated with blocking of the lymphatic channels and the accumulation of chylous material.

DR. KING: So the "thick turbid fluid" was one place where I went astray. I assumed that it was purulent, but I was not told that it was purulent.

DR. MALLORY: I did not see the fluid removed by thoracentesis. It is possible that it was purulent, but I suspect that it was similar to that which we saw a few weeks later at autopsy, which was definitely not purulent.

DR. KING: Have you often seen cancer involving the thoracic duct?

DR. MALLORY: No; it is apparently an unusual phenomenon. It is much commoner of course to see thoracic-duct occlusion from lymphomatous tumors.

DR. KING: This was not cancer over the surface of the lung.

DR. MALLORY: No; extensive cancer was present within the lung, especially in the lymphatic vessels. The right lower lobe — the one that appeared collapsed — was almost filled with carcinoma. In that lobe the cancer had invaded the bronchus. The gross picture in that area was not incompatible with primary cancer of the lung, but the rest of the pathological picture and the history ruled that out.

CASE 34032

PRESENTATION OF CASE

First admission. A twenty-one-year-old cook was admitted to the hospital because of cough, dyspnea and hoarseness.

Four months previously he developed a steady aching remitting pain that radiated to the shoulder and left arm and was unassociated with sensory or motor disturbances. It disappeared spontaneously about two months before entry, but he developed a deep chest cough, sometimes productive of white phlegm. The cough became more irritating, both day and night. In the last month he had progressive dyspnea on exertion and occasional night sweats. Two weeks before entry he developed persistent hoarseness and one week later noted intermittent pain in the right lower portion of the chest and some hemoptysis with the cough. The general condition remained good.

Physical examination revealed a well developed and well nourished man in no acute discomfort. He had obvious cough and hoarseness. The left leaf of the diaphragm was high and immobile, and in the base of the left lung the breath sounds were diminished; there were no rales. The trachea was in the midline. The superficial lymph nodes were not enlarged.

The temperature was 99°F., the pulse 90 to 100, and the respirations 20. The blood pressure was 138 systolic, 94 diastolic.

Examination of the blood disclosed a hemoglobin of 14.2 gm. and a white-cell count of 15,000, with 84 per cent neutrophils. The blood nonprotein nitrogen, the total protein and a urine examination were within normal limits.

An x-ray film of the chest revealed an irregularly ovoid, soft-tissue mass in the anterior mediastinum,

which could not be definitely separated from the heart shadow. The mass projected more to the left, where its border was poorly defined. Areas of increased density radiated from the mass into the lung. The left leaf of the diaphragm was elevated and showed limitation of movement. The left pleural cavity contained a small amount of fluid. There was a mediastinal shift to the left on inspiration.

Bronchoscopy showed paralysis of the left vocal cord in abduction. The epiglottis was normal. The trachea was pushed to the right by an intrinsic mass on the left. The caliber of the trachea and the mucosa were essentially normal. The carina was pushed a little to the right, and was slightly widened and partially fixed. The right bronchial tree was normal. The left bronchial tree could be examined only for a distance of 3 cm. beyond the carina because of fixation both laterally and medially.

An aspiration biopsy of the left side of the chest parasternally showed a few tumor cells considered to be carcinoma, but the biopsy was inadequate to warrant a definite diagnosis.

The patient was treated with 7200 r of x-ray therapy to the chest. The tumor regressed readily, and he was discharged.

Final admission (four months later). He was readmitted because of pain in the lower back radiating down the left leg to the ankle, which he had developed shortly after discharge from the hospital. He was given 1500 r of x-ray therapy to the lower spine, with questionable relief. Three weeks before entry he began to have weakness and numbness of the left leg, and two weeks later he began to have pruritus, most marked over the lower limbs. He lost about 10 pounds of weight in one month.

Physical examination revealed a well nourished man, with slight shortness of breath and hoarseness. The trachea was shifted to the left, and the breath sounds on the left were diminished. The left pupil was smaller than the right, and there was slight weakness of the left leg.

The white-cell count was 9100, with 83 per cent neutrophils. The urine showed a + test for albumin and had a specific gravity of 1.006. An x-ray film of the lumbar spine and pelvis demonstrated areas of rarefaction in the left ilium and pubic bones. In the chest there was enlargement and coalescence of the perihilar lymph nodes bilaterally, and marked elevation of the left leaf of the diaphragm.

The patient was treated with 3600 r of x-ray therapy to the pelvis and 1800 r to the chest. He vomited persistently and had a generalized Jacksonian seizure. He deteriorated progressively and died five weeks after admission.

Differential Diagnosis

Dr. Lowrey F. Davenport: We are given the salient facts in this case. A malignant tumor was discovered in the anterior mediastinum and hilar lymph nodes of the chest, causing severe localized pressure symptoms. Subsequently, it metastasized to distant parts of the body, leading ultimately to death within a period of less than a year. Our chief concern, then, is the nature of this tumor. Apparently, a presumptive diagnosis of carcinoma was accepted on the basis of the cellular findings in the chest fluid. These findings were admittedly insufficient to warrant a final diagnosis and were accepted as a working diagnosis for therapy. It may be well to review the data in chronologic order to see if a more acceptable differentiation can be made.

This twenty-one-year-old man had initial symptoms of pain in the left shoulder and arm. Two months prior to the first admission he developed a cough, followed later by dyspnea and occasional night sweats. By the time he was admitted there was hoarseness, which was due to paralysis of the left vocal cord. So far these symptoms are more consistent with a malignant lymphoma than with a primary bronchiogenic cancer. The malignant lymphomas involve hilar lymph nodes early and frequently cause early pressure symptoms. At the age of twenty-one this type of tumor is certainly more common than bronchiogenic cancer; intermittent and hectic fever is frequently associated with lymphoma, particularly of the Hodgkin type. However, we are told that the patient had had some hemoptysis just prior to admission. As a general rule lymphoma does not cause bleeding, and in contrast to bronchiogenic cancer it does not originate in the bronchial mucosa and rarely invades it. I know of no single case in which a sufficient amount of lymphomatous tissue has been obtained by bronchoscopy to make a definite diagnosis. The occurrence of hemoptysis, then, is more commonly associated with carcinoma than with lymphoma.

The physical findings give no help in the differential diagnosis at the time of the first admission. There was definite paralysis of the left vocal cord and left side of the diaphragm, which only substantiates the previous impression of a malignant tumor. The absence of enlarged superficial lymph nodes is of no diagnostic importance. We know that extensive lymphoma can occur without such adenopathy, but had it been present it would definitely be against the diagnosis of bronchiogenic cancer.

The bronchoscopic examination showed fixation of the left bronchial tree, but no intrinsic tumor was discovered. We have come to associate such fixation with malignant involvement of the mediastinal structures, but in the absence of a positive biopsy we can go no farther in differentiating various types of malignant processes.

The laboratory data, with the exception of the findings following aspiration biopsy, are of no help. Actually, in this clinic, we have had little experience in recent years with aspiration biopsy. In contrast to other clinics, it has been our usual procedure to advise exploratory thoracotomy rather than attempt

aspiration biopsy. This course has been followed because of the very same difficulty with aspiration biopsy that was encountered in this case. All too frequently insufficient tissue is obtained for diagnosis. There is also the real danger of spreading a malignant process that might otherwise be operable. In spite of this very definite lead — that "tumor cells considered to be carcinoma" were discovered — I am not yet willing to accept this statement at its face value. For the purpose of therapy, I should have agreed to large doses of x-ray radiation, believing that it was better to overtreat a lymphoma than to undertreat a cancer.

We can exclude a primary tumor elsewhere involving the chest secondarily since all the information points toward a malignant tumor originating in the chest. Among malignant tumors in the anterior mediastinum carcinomas of the thyroid gland and thymus are possibilities, but the location of this tumor was too low for these organs to be considered as sites of origin. The patient's age, the location of the tumor and the x-ray findings are against a diagnosis of bronchiogenic cancer. If we accept the aspiration biopsy as showing cancer cells, which could not be identified, we should consider a teratoma or malignant degeneration in a dermoid cyst as possibilities. Both such tumors occur commonly in the anterior mediastinum and can show a varying degree of malignancy.

However, a malignant lymphoma would best fit the entire clinical picture. This was a malignant tumor in a man of twenty-one, at which age a lymphoma is certainly the most common type of tumor. The early involvement of the hilar nodes, the initial symptoms of an irregular and unexplained fever and the widespread metastases are consistent with this diagnosis. When confronted by a single laboratory finding that does not fit the rest of the clinical picture, it is usually a safe rule to disregard it. This is even more valid when the test was admittedly "inadequate." At best our experience with aspiration biopsy has been so unsatisfactory that I should disregard this single finding and make a diagnosis of malignant lymphoma involving primarily the mediastinal lymph nodes, with widespread metastases elsewhere.

Dr. Milford D. Schulz: Films of the chest made at the first admission show a mass presenting in the left upper mediastinum, continuous with the lung root, which cannot be separated from the vascular shadows. It has an irregular ragged margin, and in the periphery of the lung, there is a homogeneous area of increased density. The left leaf of the diaphragm is elevated. A tumor mass arising in the mediastinum or in the left lung root causing paralysis of the left phrenic nerve and some patchy areas of atelectasis in the lung would look like this.

Films made after x-ray therapy show some regression of the mediastinal mass but no return of the diaphragm to normal position. Still later films of the chest demonstrate probable enlarged lymph nodes at the right lung root. A film of the pelvis made at the same time shows mottled areas of bone destruction involving the left ilium and pubis.

These findings are consistent with involvement by some malignant process. Bones involved by lymphoma look like this.

Dr. Davenport: In spite of the aspiration biopsy suggesting that the process was a carcinoma, is it not true that the type of involvement in the bones of the pelvis is unusual with carcinoma and is much more consistent with lymphoma?

Dr. Schulz: Metastatic carcinoma of the bone can have almost any appearance, but in view of the patient's age, I should consider some type of lymphoma a very likely cause for this type of destruction. The appearance is consistent with that seen in lymphoma or reticulum-cell sarcoma.

Clinical Diagnosis

Carcinoma of mediastinum.

Dr. Davenport's Diagnosis

Malignant lymphoma of mediastinal lymph nodes, with widespread metastases.

Anatomical Diagnosis

Malignant lymphoma, reticulum-cell sarcoma type, involving mediastinal and other lymph nodes, kidneys, adrenal glands, lungs, intestine, stomach, thyroid gland and bones.

Pathological Discussion

Dr. Benjamin Castleman: At post-mortem examination the mediastinum was a mass of fairly dense fibrous tissue in which could be found necrotic foci, apparently the remains of neoplastic lymph nodes. The x-ray treatment had really been effective, because the microscopical sections of most of the lymph nodes in this region showed no viable tumor.

Dr. Davenport's prediction of widespread involvement was certainly borne out. The most striking finding was a pair of kidneys with a combined weight of 2300 gm. — about six times the normal weight. They were enormous and were diffusely infiltrated with tumor, not as metastatic nodules such as one sees in carcinoma, but a generalized infiltration of the interstitial tissues deflecting and crowding out rather than destroying tubules and glomeruli. This accounts for the absence of renal failure. Similar infiltration had occurred in the lungs, adrenal and thyroid glands, stomach, small intestine and pancreas, as well as in many lymph nodes.

Morphologically, the tumor belongs to the malignant lymphoma group, and can be subclassified as a reticulum-cell sarcoma. The latter type of malignant lymphoma has a predilection for involving viscera either alone or in addition to lymph nodes and quite often misses the spleen, as was true in this case.

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WATERS DEFILED

THE London *Lancet*,* in a recent leading article, draws attention to the gross pollution of rivers and tidal reaches that exists today in Great Britain, practically unchecked. At Tynemouth, for example, the towns of Newcastle and Gateshead discharge each day approximately 30,000,000 gallons of untreated sewage into the tidal waters of the estuary — a mass of filth that requires several tides to clear away. The coastline of 150 miles between Liverpool and Barrow is the daily recipient of 200,000 gallons of crude sewage per mile, or about forty bucketsful per yard. In these waters people bathe by the thousands in hot weather, and from them shrimps and prawns are harvested for the nation's tables.

*Leading article. Filthy rivers. *Lancet* 2:58, 1947.

Interestingly enough, it is the British angler who is making the greatest outcry over this situation, for his salmon are disappearing, but Parliament will shortly have an opportunity to take cognizance of the situation when it considers the Rivers Boards Bill containing the recommendations of the Central Advisory Water Committee.

We have no superiority in this respect in our own country about which to brag, for we, too, have contaminated our streams and polluted our beaches without regard to health, decency or esthetic considerations. Harold L. Ickes in his column in *The Boston Traveler* of September 25, 1946, presents some figures that give an account of our stewardship over this land that spreads from sea to shining sea.

"More than 3400 cities and towns," he writes, "inhabited by 29,000,000 persons discharge into our waterways a volume of 2½ billion gallons of raw sewage plus 3¾ billion gallons of industrial waste each day. . . . The annual economic loss resulting from water pollution has been variously estimated at from a hundred million to a billion dollars."

Massachusetts made at least a start in the control of water pollution in 1945, when the Legislature authorized the Department of Public Health to prescribe rules and regulations "to prevent pollution of lakes, ponds, streams, tidal waters and flats and tributaries thereto." In certain instances it has been necessary to prosecute recalcitrant offenders before health hazards could be prevented and nuisances abated. In others, industrial wastes had become so obnoxious that living conditions in the vicinity were unbearable, and even the paint on buildings was discolored by gases containing hydrogen sulfide.

In 1947 further remedial measures were taken with the passing of legislation in Massachusetts, Connecticut and Rhode Island authorizing the ratification of a proposed compact between these states and the other New England states for the abatement of existing pollution and the control of future pollution in interstate waters. Putting these measures into execution will be slow, however, because of the costs involved and the scarcity of labor and materials for the construction of treatment works.

VOLUNTARY HEALTH AGENCIES AND THE NATIONAL HEALTH COUNCIL

THE need for co-ordination and co-operation among voluntary health agencies, particularly at the community level, has long been recognized. A cogent statement of proposals for greater efficiency that also contains an analysis of the problems and opportunities inherent in this phase of public health[1] was recently adopted by the National Health Council as a guide in the future development of its activities. If properly carried out any program based on the principles advocated in this memorandum should go far toward lightening the burden of illness, accident and premature death and, incidentally, toward eliminating the ever-present bugbear of governmental interference in medicine and public health. Proposals directed toward the attainment of such a goal merit the careful attention of all members of the medical profession.

The essential features of a local health council are defined as follows: representation of all operating health agencies in the community, both official and voluntary; continuous opportunity to study health needs and to assess health problems and work together on their solution; and an atmosphere of co-operation and tolerance for all members. The unified support of all voluntary agencies combined in a council is held to offer a great advantage to local health departments.

Existing health agencies struggling with identical problems will welcome advice (but not dictation) from a national source that is familiar with successful public-health methods throughout the country. Therefore, the closest co-operation of function among all health organizations is urged, but the idea of interfering with methods of fund raising or merging the functions of various agencies at the national level is rejected. The role of the National Health Council in this scheme for more efficient operation is regarded as vital, and it is recommended that the Council, which already comprises representation of such major organizations as the National Tuberculosis Association, American Red Cross, American Cancer Society, American Public Health Association and National Organization for Public Health Nursing,[2] be expanded to include the Health Section of the Office of Education. the National Foundation for Infantile Paralysis, the American Medical Association (formerly a member), the American Hospital Association and other professional groups. Other recommendations include the establishment and expansion of a central statistical service and provision for a library and information service, since the National Health Council is not only in an advantageous position to observe and evaluate reports from all parts of the country and to suggest promising directions for further investigation but also especially fitted to stimulate sociologic and administrative research, which has lagged behind the more basic scientific investigations.

The specific proposals are based on the conviction that permanent progress in public health can best be achieved if people are helped to recognize and to solve their own health problems. The cordial attitude of the public toward health guidance and health agencies, the existence of more numerous and more competent bodies of health workers than ever before and the advantage of modern technics and scientific advances are considered to offer an unprecedented opportunity for constructive efforts to attain the goal of optimum health for the greatest number of people. The guiding principles proposed for the staff of the National Health Council are as follows: "field work; counselling and co-operation within and without; decentralization at every opportunity; focusing on problems, not on personalities; receptiveness to new ideas and to local viewpoints; suggestion rather than oracularity; a viewpoint broad enough to encompass the special interests of all health agencies, both voluntary and official; realization that many local health agencies are doing superior work and can contribute much to the national agencies."

Dr. W. P. Shepard, author of these proposals and president of the National Tuberculosis Association, deserves the highest praise for a clear and constructive outline of public-health needs. The recommendations, essentially, apply the principle of the Community Fund to all matters pertaining to health. The progress of the National Health Council in forwarding the implementation of these suggestions will be closely watched by physicians and laymen alike, for the stake involved — mainte-

nance and improvement of health by democratic means — is vital.

REFERENCES

1. Shepard, W. P. Unpublished memorandum to National Health Council, dated August 1, 1946.
2. Medical News. National Health Council expands program. *J. A. M. A.* 133:629, 1947.

"THAT THESE HONORED DEAD"

A FUNERAL procession has begun this year that will consume five more before its ending. Coming from the four quarters of the globe its various elements are converging on their homeland bearing the bodies of our dead of World War II.

Congress has voted this posthumous repatriation and reburial, and the next of kin must make the decision whether to leave the body of the deceased where it was buried by his comrades or to bring it home for reinterment. The soldier or the sailor cannot be consulted. He has made his last decision on all matters earthly.

The *Journal* published on November 13, 1947, a directive from the Department of Public Health regarding the technicalities of reburial in the Commonwealth, giving grim substance to this sentimental journey, and the relatives of more than 200,000 servicemen who lie buried in foreign soil have signified their desire to have the bodies returned. There are those who feel that the deceased would wish to remain where he now is; others prefer that their relative shall rest in the homeland and this, too, is entirely fitting and proper.

There may be many reasons given either for exhuming these unembalmed bodies and bringing them home for reburial or for leaving them in permanent United States military cemeteries abroad. The ultimate reason is one of sentiment, whether the body shall lie in a grave that can be watched and tended by those of his own blood or rest in a bit of American soil in some other country — a sentiment once so fittingly expressed in the familiar words of Rupert Brooke: "That there's some corner of a foreign field that is forever England."

However we may feel in this respect, there comes the thought that wherever "these honored dead" may lie, it is "for us, the living" still to show that "increased devotion to the cause for which they gave their last full measure of devotion."

Wherever they may lie, may we be stimulated to greater efforts to see that out of the destruction of war there shall come something better for those now living!

THE NEW ENGLAND DENTAL JOURNAL

The *New England Journal of Medicine* welcomes into the ranks of scientific journalism the *New England Dental Journal*, as the official publication of the six New England dental societies.

The *New England Dental Journal*, a logical successor to the *Massachusetts Dental Society Bulletin*, which has been in publication since 1924, is making its bow with the new year. Its publication will be in the hands of a representative committee composed of an editor from each New England state, under the two-year chairmanship of Dr. Cedric F. Harring, of Brookline, Massachusetts. Dr. Harring has been editor of the *Massachusetts Dental Society Bulletin* since January, 1945.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BAILEY — Karl R. Bailey, M.D., of Jamaica Plain, died on December 21. He was in his sixty-first year.

Dr. Bailey received his degree from Tufts College Medical School in 1910. He was deputy health commissioner for the City of Boston and was a former member of the Massachusetts Medical Society.

His widow and two daughters survive.

McDONALD — Ray T. McDonald, M.D., of Medford, died on December 5. He was in his sixty-second year.

Dr. McDonald received his degree from Tufts College Medical School in 1918. He was senior medical officer at the Lawrence Memorial Hospital, Medford, and a fellow of the American Medical Association.

His widow, a son, a daughter and a brother survive.

MacGRAY — Charles L. MacGray, M.D., of Needham, died on December 25. He was in his sixty-eighth year.

Dr. MacGray received his degree from Tufts College Medical School in 1914. He was a member of the New England Pediatric Society and a fellow of the American Medical Association.

His widow, a son, five daughters, two brothers and six sisters survive.

PHILLIPS — Charles H. Phillips, M.D., of Beverly, died on December 22. He was in his seventy-seventh year.

Dr. Phillips received his degree from Bowdoin Medical School in 1900. He was formerly assistant medical examiner for Essex County and was a fellow of the American Medical Association.

His widow, two daughters and three grandchildren survive.

PICKARD — Isaiah L. Pickard, M.D., of West Concord, died on August 12. He was in his eighty-first year.

Dr. Pickard received his degree from Harvard Medical School in 1896. He was a former member of the Massachusetts Medical Society.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

SCHEDULING IMMUNIZATIONS

So many considerations enter into determining the order and the age for the administration of immunizations that there is as yet no general agreement regarding an ideal plan.

The present recommendations of the Department concerning such schedules are given in Table 1.

TABLE 1. *Immunization Procedure Recommended.*

DISEASE	AGE AT TIME OF INITIAL DOSE	PRODUCT (ANTIGEN)	DOSE	INTERVAL BETWEEN DOSES	BOOSTER DOSE OR REIMMUNIZATION	REMARKS
	mo.			*days*		
Whooping cough	3–6	Pertussis vaccine	Three doses of plain vaccine (80,000,000,000 bacilli); alum-precipitated vaccine (30,000,000,000 bacilli).	30	One dose 1 yr. later; repeated at 5–6 yr.; plain vaccine (20,000,000,000 bacilli); alum-precipitated vaccine (10,000,000,000 bacilli).	Vaccine may be combined with diphtheria toxoid; booster doses should be given when disease is prevalent.
Smallpox	3–6	Smallpox vaccine	One vaccination	—	At 5–6 yr. of age§ every 5–10 yr. thereafter.	Vaccine may be combined with any dose of pertussis vaccine; revaccination indicated when disease is prevalent.
Diphtheria	6–9	Diphtheria toxoid*	Three doses of 0.5, 1.0 and 1.0 cc.§	21–30	One dose (0.5 cc.) at 5–6 yr. of age§	Booster doses should be given at shorter intervals when diphtheria is prevalent
Tetanus	6–12	Tetanus toxoid	Two doses of 1.0 cc. each	30	Recall dose (1.0 cc.) 1 yr. later	Another dose indicated after each deep or contaminated wound
Typhoid fever	(When advised by physician)	Typhoid vaccine	Three doses of 0.5, 1.0 and 1.0 cc.‡	7–10	One dose (0.5 cc.) annually in areas where needed†	Triple vaccine should be given to travelers

*Two doses, 30 days apart, should be used for alum-precipitated toxoid.

†For booster dose, 0.1 cc. intracutaneously can be used.

‡Three doses of 0.5 cc. each recommended by some.

§For adolescents and adults, the first dose of diphtheria toxoid should be 0.1 cc., the size of succeeding doses being gauged by the reaction from the first inoculation.

These recommendations will be amended as new knowledge on many points is brought forward.

If every family followed a schedule of this kind, these diseases would become of little importance in Massachusetts.

Because parents often neglect to have the immunizations done by their own physicians, boards of health have been compelled to organize community immunization programs. In such programs, departure from the recommended procedures must occasionally be made. The essentials, however, can easily be covered in these programs.

HARVARD PUBLIC HEALTH CHEST CLINIC

The official opening on Friday, November 7, of the Harvard Public Health Chest Clinic, located in the former Huntington Memorial Hospital, now part of the Harvard School of Public Health, marked a new step in co-operative tuberculosis prevention. By pooling funds, equipment and personnel, the Harvard Public Health Chest Clinic was brought into existence to serve the Peter Bent Brigham Hospital, Boston Lying-In Hospital, Children's Hospital, Harvard Medical School and Harvard School of Public Health.

The unit is under the direction of Dr. Merrill C. Sosman, radiologist at the Peter Bent Brigham Hospital. Other personnel and equipment are provided by the Massachusetts Department of Public Health through grants from the Tuberculosis Control Division of the United States Public Health Service.

Through the use of 70-mm. photofluorographic equipment, the cost of operation has been reduced to the extent that the project is economically feasible.

The objective is to provide routine x-ray examinations of patients and employees of the member hospitals, as well as students and employees of Harvard Medical School and Harvard School of Public Health.

Since it has been shown that the tuberculosis rate of patients in general hospitals is approximately twice that of persons in the ordinary population, it is hoped that the routine screening for tuberculosis as proposed in this program will prove an effective means of disclosing unrecognized cases and protecting the hospital employees, medical-school personnel and nurses.

MISCELLANY

NOTES

The following appointments to the teaching staff of Harvard Medical School were recently announced: René Tagnon, of Brussels, Belgium (A.B. University of Brussels 1939; M.D. University of Liège Medical School 1943), research fellow in medicine; Albert Kam Tai Ho, of Honolulu, Hawaii (S.B. University of Hawaii 1937; M.D. Jefferson Medical

College 1942), assistant in laryngology; Raymond Frank Kuhlmann, of Milwaukee, Wisconsin (A.B. University of Wisconsin 1936; M.D. Washington University 1939), assistant in orthopedic surgery; Herbert Fanger of Brookline (A.B. Harvard University 1936; M.D. New York Medical College 1940), assistant in pathology; Arthur Burns of Brighton (S.B. Boston College 1922; M.D. Tufts College Medical School 1926), teaching fellow in radiology; Chun-Hsiang Liu, of Peiping, China (M.B. Ministry of Education, China 1940; M.D. National Tung Chi University Medical School Shanghai 1941; D.T.M. Calcutta School of Tropical Medicine 1945), research fellow in physical chemistry; Robert Fernand Mouton, of Brussels, Belgium (S.D. Brussels Free University 1944), research fellow in physical chemistry; Hans Nitschmann, of Berne, Switzerland (Ph.D. University of Berne 1931); (Privatdozent University of Berne 1942), research fellow in physical chemistry; Charles Tanford, of Boston (A.B. New York University 1943; A.M. Princeton University 1944; Ph.D. Princeton University 1947), research fellow in physical chemistry; Eero Johannes Uroma, of Helsinki, Finland (M.D. University of Helsinki 1943; Privatdozent Sero-Bacterioloģe, Helsinki, 1947), research fellow in physical chemistry; Luis Saenz-Arroyo, of Mexico, D.F. (S.B. Institut Franco-Anglais 1937; M.D. National University of Mexico D.F.), research fellow in neurology; Lloyd Irving Sexton, of West Newton (S.B. Tufts College 1939; M.D. Boston University School of Medicine 1943), research fellow in obstetrics; Harry Amerman Bliss of Buffalo, New York (A.B. Princeton University 1941; M.D. Harvard University 1944), research fellow in physiology; John Lu, of Nanking, China (V.Sc. West China Union University 1940; M.D. West China Union University 1945), research fellow in surgery; John Eric Richardson, of Leicestershire, England (M.B. London Hospital Medical College 1939; M.S. London Hospital Medical College 1941; F.R.C.S. London Hospital Medical College 1944), research fellow in surgery; Joseph Worcester Spelman, of Kent, Connecticut (M.D. Yale University 1944), research fellow in legal medicine; John William Raker, of Boston (S.B. Bucknell University 1937; M.D. Harvard University 1941), research fellow in biologic chemistry; and Ian Chester Jones, of Liverpool, England (B.Sc. Liverpool University 1938; Ph.D. University of Liverpool 1941), research fellow in dental science.

NATIONAL CANCER INSTITUTE OF THE UNITED STATES PUBLIC HEALTH SERVICE

Awards totaling nearly $750,000 in National Cancer Institute grants have been announced in a report made public by Dr. Thomas Parran, Surgeon General of the United States Public Health Service. Altogether 46 grants for clinical and basic biologic research were given on the recommendation of the National Advisory Cancer Council, composed of outstanding authorities on cancer from various sections of the country.

For the first time in the ten-year history of the Council grants were given to scientists working outside this country. The two recipients were Dr. A. Lacassagne, of the Institute Pasteur in Paris, who received $13,380, and Dr. L. Doljanski, of Hebrew University in Palestine, who received $10,000.

AMERICAN COLLEGE OF PHYSICIANS RESEARCH FELLOWSHIPS IN MEDICINE

Research fellowships in medicine, with stipends ranging from $2200 to $3200, have been awarded by the American College of Physicians to the following physicians, for the year beginning in July: Charles G. Campbell, of Vancouver, B. C., for studies of the basic physiology of certain cardiovascular problems (at McGill University Faculty of Medicine); Frank H. Gardner, of San Bernardino, California, for studies of the mechanism and clinical application of the osmotic fragility test (at the Thorndike Memorial Laboratory, Boston City Hospital); Samuel P. Martin, of Durham, North Carolina, for studies of bacterial metabolism (at the Rockefeller Institute for Medical Research, New York City); Peritz Scheinberg, of Miami, Florida, for studies of cerebral circulation and peripheral vascular flow in normal and hypertensive persons (at Duke University Hospital); Lutfu Lahut Uzman, of Istanbul, Turkey, for studies of the isolation and characterization of brain proteins and their role in health, disease and senescence (at the Department of Scientific Research, McLean Hospital, Waverley, Massachusetts); and John M. Weller, of Ann Arbor, Michigan, for studies of the ionic patterns of intracellular fluids and their influence on enzymatic reactions and of acid-base balance in tissues other than skeletal muscle tissues (at the Department of Biologic Chemistry, Harvard Medical School).

INDUSTRIAL CONFERENCE ON ALCOHOLISM

The first Industrial Conference on Alcoholism will be held in the Morrison Hotel, Chicago, on Monday, March 15. Sponsored by the Chicago Committee on Alcoholism, the Conference has been designed to bring to the attention of industrial leaders throughout the country facts pertaining to the problem of alcoholic employees and to discuss ways and means of overcoming the problem.

The Conference has been divided into three parts. In the morning session the discussion will center around "The Problem."

The second session will be held at a special luncheon at which an outstanding authority on the subject will be the key speaker. The afternoon session will cover the subject "What To Do about the Problem."

Reservations for attending the technical sessions and the luncheon may be made by application in writing to Walter O. Cromwell, vice-president, Chicago Committee on Alcoholism, 816 South Halsted Street, Chicago 7, Illinois.

"THIS WEEK IN CHICAGO MEDICINE"

The Chicago Medical Society has inaugurated a weekly mimeographed publication entitled "This Week in Chicago Medicine," designed to keep the medical profession posted and to aid out-of-town physicians who wish to visit clinics, conferences, round tables or medical meetings in Chicago.

Any doctor planning a trip to Chicago may obtain copies of this bulletin by writing to the Chicago Medical Society, 30 North Michigan Avenue, Chicago 2, or by calling in person.

BOOK REVIEWS

Hypnotism Today. By Leslie M. Lecron, B.A., and Jean Bordeaux, M.A., Ph.D. With a foreword by Milton H. Erickson, M.D. 8°, cloth, 278 pp. New York: Grune and Stratton, 1947. $4.00.

The expressed purpose of this book is to "demonstrate . . . that hypnotism is a true branch of psychological science, and to aid in removing some of the last lingering traces of the esoteric which still cling to it." So far as the authors adhere to the topic of hypnosis they do well in presenting the historical background and in offering critiques of existent laboratory studies, but these critiques are for the most part empirical and subjective. However, the authors digress at great length, with frequent interjections from their own experiences, into summary descriptions of behavior abnormalities (nonpsychotic), depiction of systems of psychotherapy in present vogue and further ramifications into the emotionally fraught question, In whose bailiwick lies psychotherapy? They make out a plausible case for hypnosis ancillary to psychoanalysis (nonorthodox).

In many respects this volume has merit: in its suggestions for measuring depth of the hypnotic state, in pointing out various weaknesses in past studies and present application and in offering leads for future research. The excursions across other horizons create a fog through which the title subject looms only occasionally. The authors in their zeal become somewhat evangelical and lose effectiveness through this disunity. The book ends with observations and philosophical conjecturing on the present training of physicians (psychiatrists) and psychologists (clinical psychologists) and equivocating about definitions of psychotherapy and treatment.

The book is easily read, and when the authors adhere to the title they present suggestions from their empirical experience that may be of value in stimulating objective work with hypnosis. The volume contains one hundred and twenty-six references and an index.

Diseases of the Chest: Diagnosis and treatment. By Archibald R. Judd, M.A., M.D. 8°, cloth, 608 pp., with 140 illustrations. Philadelphia: F. A. Davis Company, 1947. $9.00.

In his preface the author outlines the objective of this book as a concise, practical and systematic manual of diseases of the chest. He emphasizes the fact that he wrote it to fill the needs of the general practitioner, intern or medical student, and not for the specialist. It is with this in mind that the reviewer has gone over the twenty-seven chapters of this manual.

There are five parts that consider the anatomy and physiology of the thorax, a fairly exhaustive study of pulmonary tuberculosis, nontuberculous pulmonary suppuration, diseases of the lungs and pleura, such as silicosis, neoplasms, fungous diseases and cystic disease, and finally miscellaneous aids in diagnosis, including bronchoscopy, bronchography and various other laboratory aids.

The author has long been a recognized authority on diseases of the chest and has absorbed much of the enthusiasm and zeal in the study of bronchology and pulmonary diseases from his close associates, the Jacksons. As a result of this major interest of the Philadelphia group there has certainly evolved, in the past quarter of a century, a much better and clearer concept of the physiology, pathology and rational treatment of lung diseases. The author discusses the subject quite adequately, with an excellent interpretation of the long background and his personal experience in lung diseases.

Unfortunately, books do not have a morning and evening edition. In this atomic age there is nothing more perishable than a book on practical treatment. Some of the procedures are outmoded before the book reaches the shelves of the bookstore. Thus, the omission of streptomycin in the general scheme of therapy in pulmonary tuberculosis is bound to leave quite a vacuum. Undoubtedly, streptomycin is here to stay, and the entire early treatment, especially that of tracheobronchial tuberculosis and other tuberculous complications, will have to be reconsidered. In the light of present knowledge the entire chapter on tuberculous bronchitis will have to be rewritten immediately.

Likewise, the chapter on carcinoma of the lungs lacks the latest procedures of bronchoscopic aspirations and the newer staining methods, which make early diagnosis possible in a much higher percentage of cases.

The place of lobectomy and pneumonectomy in pulmonary tuberculosis is much more clearly defined now, in view of the newer armamentariums on the treatment of pulmonary diseases. The remarks presented above are not meant as a criticism of the book, but point to the need of a new edition almost before the ink has had a chance to dry.

Aside from the few omissions outlined, the author has covered the ground of all chronic diseases of the chest in a very adequate and practical manner. The general practitioner will find it an excellent reference book, and the medical student will find it very useful as a condensed manual of all chest diseases. It is certainly a welcome addition to the literature on diseases of the chest.

Signs and Symptoms: Their clinical interpretation. Edited by Cyril M. MacBryde, M.D. 4°, cloth, 439 pp., with 74 illustrations and 6 plates. Philadelphia: J. B. Lippincott Company, 1947. $12.00.

The title of this unusually well organized, composite work defines clearly the objective of the authors — namely, to impress the physician with the importance of understanding correctly the complaints for which the patient consults him. With such an understanding a careful clinical history not only will simplify the physical examination and the selection of specialized laboratory tests but also will determine in large measure the correct diagnosis and appropriate treatment.

After an introduction by the editor on the art of history taking and on the technic of interpreting symptoms there follow twenty-six sections or chapters covering nearly the entire field of symptomatology. Because pain is by far the most common presenting symptom, a third of the book is devoted to this subject in its various manifestations: headache, sore tongue and mouth, thoracic, abdominal, back and joint pain and pain in the extremities. Next are taken up fever, fainting and convulsions, dyspnea, cyanosis, palpitation, cough and hemoptysis, edema and dehydration, anorexia, vomiting and hematemesis, constipation, diarrhea and melena, jaundice, itching and, finally, nervousness and fatigue. Because the list is so comprehensive it is surprising that symptoms such as vertigo, purpura and hematuria have not been included.

Each section is a finished monograph in itself, concise and well correlated with the rest. The mechanism of each major symptom is clarified by whatever bearing anatomy, pathology, physiology, chemistry or psychology may have on it, and its correlation with other symptoms and with physical and laboratory findings is emphasized. The text is illustrated with many charts, diagrams and photographs in black and white and in color. References follow each section. Local contributors are Sara M. Jordan and William G. Lennox.

All in all this comprehensive work fulfills well the objective of the authors to help the physician evaluate the signs and symptoms of disease so that he may reach a correct diagnosis.

Concise Anatomy. By Linden F. Edwards, Ph.D. 4°, cloth, 548 pp., with 324 illustrations. Philadelphia: The Blakiston Company, 1947. $5.50.

This book admirably fulfills its intention to teach the basic principles of human anatomy to students in fields ancillary to medicine, such as nursing and physical education. It supplants the previous text by the same author entitled *Anatomy for Physical Education.* Much new material has been added, and the author correlates the anatomy with physiology and other applied matters. Although it is concise and simply written, the volume is entirely scientific in its approach and is obviously directed to people at college level. The illustrations and format are both instructive and pleasing, and the book can be heartily recommended for students in the fields mentioned above.

Diseases of the Gallbladder and Allied Structures: Diagnosis and treatment. By Moses Behrend, M.D. With a foreword by Thomas A. Shallow, M.D. 8°, cloth, 290 pp., with 110 illustrations. Philadelphia: F. A. Davis Company, 1947. $7.00.

This book is a review of forty-five years' experience in the medical and surgical management of diseases of the gall bladder, bile passages and pancreas.

In the chapter on interpretation of liver-function tests, the limitations of the tests and their optimal value during the course of jaundice and convalescence are not included. It is stated that the urobilinogen in the urine is increased in hepatocellular jaundice. However, in the reviewer's experience this urinary pigment may be present in low levels or absent during the acute hepatocellular jaundice and in increased amounts only at the onset or at convalescence of the disease, when bile pigment is present in large quantity in the intestine. This test is frequently not of much help during the height of the illness, because the severely damaged liver may not be capable of manufacturing bile pigments. Its outstanding value is in revealing the patency of the common bile duct.

The omission of the value of the simple hippuric acid test as an indication of dehydration in the preoperative preparation of the patient with cholecystitis was probably an oversight.

The statement that persistent hypoprothrombinemia, in spite of adequate intramuscular administration of vitamin K, is a differential point excluding obstructive jaundice in favor of acute hepatocellular jaundice is not valid. In a large series of both obstructive and acute hepatocellular cases the responses of hypoprothrombinemia to vitamin K were approximately the same. Persistent hypoprothrombinemia, in spite of adequate vitamin K, occurred in chronic parenchymatous hepatitis and was usually an unfavorable prognostic sign.

None of the function studies described have revealed liver damage in the presence of severe grades of congestive heart failure.

The potential danger of increased liver damage if sulfonamides are used in jaundiced patients is over-rated. The low incidence of sulfonamide sensitivity makes the use of these drugs relatively innocuous.

Recommendation of the indiscriminate use of plasma in preoperative preparation without knowledge of the source of the plasma may well result in more cases of homologous serum hepatitis, some of which are fulminating.

Anatomic variations and recent operative procedures are very well illustrated. The diagnosis and treatment of cholecystitis and pancreatic diseases are well outlined.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Twenty-Four-Hour Variations of Gastric Function and Their Significance for Diagnosis, Prophylaxis and Treatment of Dyspepsia, Especially in Tuberculosis. By Erik Forsgren, M.D., physician-in-chief, Svenshögen County Sanatorium. 4°, paper, 34 pp. Lund, Sweden: Hakan Ohlssons Boktryckeri, 1946.

This study is based on routine examinations of 120 sanatorium patients, who were divided into two main groups: those with homoacidity and those with heteroacidity. They were studied on the basis of correlation between gastric acidity and subjective symptoms of dyspepsia and the correlation of tuberculosis and gastric function. The development of achylia and anemia associated with tuberculosis and the significance of the twenty-four-hour variation of gastric function from both the diagnostic and the hygienic viewpoints are discussed at length. A section is devoted to the treatment of achylia, especially in tuberculous subjects. The paper concludes with a summary in which the author states that he believes that routine examination of twenty-four-hour variations of gastric function should be made if there are symptoms of peptic ulcer, indigestion, deficiency conditions or tuberculosis.

The Years After Fifty. By Wingate M. Johnson, M.D., professor of clinical medicine and chief of private diagnostic clinic, Bowman Gray School of Medicine, Wake Forest College. With a foreword by Morris Fishbein, M.D. 8°, cloth, 153 pp. New York: McGraw-Hill Book Company, Incorporated, $2.00.

During the past few years a number of popular books have been written on the hygiene and management of old age. Dr. Johnson has added another to this growing series and seemingly has not been able to reach down to the level of the layman but has landed in the middle between the physician and the subject. The style is factual and not conducive to easy interesting reading. The short comments are more on the professional than on the lay level.

A Manual of Fractures and Dislocations. By Barbara B. Stimson, M.D., M.Sc.D., assistant professor of clinical orthopedic surgery, College of Physicians and Surgeons, Columbia University, and associate attending surgeon, Presbyterian Hospital and Vanderbilt Clinic, New York City. Second edition. 12°, cloth, 223 pp., with 98 illustrations. Philadelphia: Lea and Febiger, 1947. $3.25.

This manual has been revised in the light of war experience and has been brought up to date especially in the field of treatment. It should prove useful for ready reference to student and practitioner alike.

Advances in Pediatrics. Volume II. 8°, cloth, 409 pp., with 84 illustrations. New York: Interscience Publishers, Incorporated, 1947. $6.75.

This second volume presents eleven special monographs on pediatric subjects of diversified interest and should prove valuable to the physician, as well as the pediatrician. The subjects discussed include the etiology of congenital malformations, endocrine and other factors determining the growth of children, prematurity, physiologic hyperbilirubinemia, the prevention of recurrences of rheumatic fever, acute infectious lymphocytosis, treatment of purulent meningitides, virus diarrhea, atypical pneumonia, the role of fluorine in prevention and treatment of dental caries and chemotherapy, including penicillin, the sulfonamides, streptomycin and tyrothricin. The papers are well written and provide up-to-date information on the various subjects. The book is well published in every way and should be in all medical libraries.

Psychiatric Research. Papers read at the dedication of the Laboratory for Biochemical Research, McLean Hospital, Waverley, Massachusetts, May 17, 1946. By Cecil K. Drinker, M.D., Sc.D., Jordi Folch, M.D., Stanley Cobb, M.D., Herbert S. Gasser, M.D., Sc.D., LL.D., Wilder Penfield, C.M.G., M.D., Sc.D., F.R.S., and Edward A. Strecker, M.D., Sc.D. 8°, cloth, 113 pp. Cambridge, Massachusetts: Harvard University Press, 1947. $2.00. *Harvard University Monographs in Medicine and Public Health*, No. 9.

The seven papers comprising this volume are written by outstanding authorities in their particular fields. Dr. Drinker writes on research at the McLean Hospital, Dr. Folch on biochemical problems related to psychiatry, Dr. Stanley Cobb on the integration of medical and psychiatric problems, Dr. Gasser, director of the Rockefeller Institute, on a protocol for a review of psychiatry, Dr. Penfield, of McGill University, Montreal, on psychical seizures, and Dr. Strecker, of the University of Pennsylvania on the psychobiology of psychiatric research. This volume should be in all medical libraries and in all institutions having to do with mental disease. The small volume is published in the usual fine style of the Harvard University Press.

NOTICES

ANNOUNCEMENTS

Dr. Max Ettenberg announces the removal of his office to 258 Harvard Street, Cambridge.

Dr. Stanley J. G. Nowak announces the opening of his office for the practice of surgery at 99 Commonwealth Avenue, Boston.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, January 20, at 8:15 p.m. A symposium on "Recent Advances in Chemotherapy" will be presented. Dr. Chester S. Keefer will be chairman.

PROGRAM

Treatment of Pneumonia and Meningitis, with Some Consideration of Modern Trends in Time-Dose Relations in Antibiotic Therapy. Dr. Maxwell Finland.

Antibiotic Therapy in Scarlet Fever and Diphtheria, with a Consideration of the Change in Bacterial Flora of Infections during and following Treatment. Dr. Louis Weinstein.

Role of Streptomycin in the Treatment of Urinary-Tract Infections, with a Consideration of Its Toxicity. Dr. William L. Hewitt.

LOWELL LECTURES ON THE HOSPITAL IN CONTEMPORARY LIFE

The following lectures, which comprise the second half of a course of eight Lowell Lectures on the subject "The Hospital in Contemporary Life," will be given in the Lecture Hall, Boston Public Library, Copley Square, Boston, at 8 p.m. on the days indicated:

Tuesday, January 20. The Education of the Doctor. Dr. Oliver Cope.

Friday, January 23. How Medicine Grows and Its Relation to Science. Dr. Eugene M. Landis.

Tuesday, January 27. Unsolved Problems. Dr. Joseph C. Aub.

Friday, January 30. The Place of the Hospital in the Social Order. Dr. Nathaniel W. Faxon.

Tickets can be obtained by mail, in advance, from the Curator of the Lowell Institute, Boston Public Library, from the office of the Director, Massachusetts General Hospital, or at the door immediately before each lecture.

(*Notices concluded on page xiii*)